Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Ticarcillin Disodium Powder for Injection (contains 4.75 mEq sodium/g) and Clavulanate Potassium (contains 0.15 mEq potassium/g): 3 g ticarcillin and 0.1g clavulanic acid in 3.1 g vials, piggyback bottles, ADD-Vantage vials and 31 g pharmacy bulk packages; *Timentin®* (GlaxoSmithKline); (Rx)

Ticarcillin Powder for Injection (contains 18.7 mEq sodium/100 mL) and Clavulanate Potassium (contains 0.5 mEq potassium/100 mL): 3 g ticarcillin and 0.1 g clavulanic acid/100 mL in 100 mL premixed, frozen Galaxy plastic containers; *Timentin®* (GlaxoSmithKline); (Rx)

TILETAMINE HCL/ZOLAZEPAM HCL

(tye-***let***-a-meen and zoe-***laze***-a-pam) Telazol®

INJECTABLE ANESTHETIC/TRANQUILIZER

Prescriber Highlights

- Injectable anesthetic/tranquilizer combination similar to ketamine/diazepam
- Contraindications: Pancreatic disease, rabbits, severe cardiac disease, use in cesarean section, or pulmonary disease
- Caution: Renal disease, large exotic cats (use avoided)
- Protect patient's eyes after using
- Dosages may need to be reduced in geriatric, debilitated, or animals with renal dysfunction.
- Adverse Effects: Respiratory depression, pain after IM injection, athetoid movements, tachycardia (esp. dogs), emesis during emergence, excessive salivation & bronchial/tracheal secretions, transient apnea, vocalization, erratic &/or prolonged recovery, involuntary muscular twitching, hypertonia, cyanosis, cardiac arrest, pulmonary edema, muscle rigidity, & either hypertension or hypotension
- Monitor body temperature (may cause hypothermia)
- Class-III controlled substance

Uses/Indications

Telazol® is indicated for restraint or anesthesia combined with muscle relaxation in cats, and for restraint and minor procedures of short duration (≈30 minutes) which require mild to moderate analgesia in dogs. Although not officially approved, it has been used also in horses and many exotic and wild species.

Pharmacology/Actions

In cats, tiletamine decreases cardiac rate and blood pressure after IM injections. Its effect on respiratory activity is controversial, and until these effects have been clarified, respiratory function should be closely monitored. The pharmacology of this drug combination is similar to that of ketamine and diazepam; for more information, refer to their monographs.

Pharmacokinetics

Little pharmacokinetic information is available for these agents. The onset of action may be variable and be very rapid; animals should be observed carefully after injection.

In cats, the onset of action is reported to be within 1–7 minutes after IM injection. Duration of anesthesia is dependent on dosage, but is usually about 0.33–1 hour at peak effect. This is reported to be approximately 3 times the duration of ketamine anesthesia. The duration of effect of the zolazepam component is longer than that of the tiletamine, so there is a greater degree of tranquilization than anesthesia during the recovery period. The recovery times vary in length from approximately 1–5.5 hours.

In dogs, the onset of action following IM injection averages 7.5 minutes. The mean duration of surgical anesthesia is about 27 minutes, with recovery times averaging approximately 4 hours. The duration of the tiletamine effect is longer than that of zolazepam, so there is a shorter duration of tranquilization than there is anesthesia. Less than 4% of the drugs are reported excreted unchanged in the urine in the dog.

Contraindications/Precautions/Warnings

Telazol® is contraindicated in animals with pancreatic disease, or severe cardiac or pulmonary disease. Animals with renal disease may have prolonged duration of anesthetic action or recovery times.

Because *Telazol®* may cause hypothermia, susceptible animals (small body surface area, low ambient temperatures) should be monitored carefully and supplemental heat applied if needed. Like ketamine, *Telazol®* does not abolish pinnal, palpebral, pedal, laryngeal, and pharyngeal reflexes and its use (alone) may not be adequate if surgery is to be performed on these areas.

It has been reported that this drug is contraindicated in rabbits due to renal toxicity.

Telazol® is generally avoided for use in large, exotic cats (contraindicated in tigers) as it may cause seizures, permanent neurologic abnormalities, or death.

Cats' eyes remain open after receiving *Telazol®*, and they should be protected from injury and an ophthalmic lubricant (*e.g.*, *Lacrilube®*) should be applied to prevent excessive drying of the cornea. Cats reportedly do not tolerate endotracheal tubes well with this agent.

Dosages may need to be reduced in geriatric, debilitated, or animals with renal dysfunction.

Adverse Effects

Respiratory depression is a definite possibility, especially with higher dosages of this product. Apnea may occur; observe animal carefully. Pain after IM injection (especially in cats) has been noted which may be a result of the low pH of the solution. Athetoid movements (constant succession of slow, writhing, involuntary movements of flexion, extension, pronation, etc.) may occur; do not give additional *Telazol®* in the attempt to diminish these actions. Large doses given SC or IM, versus small doses given IV, may result in longer, rougher recoveries.

In dogs, tachycardia may be a common effect and last for 30 minutes. Insufficient anesthesia after recommended doses has been reported in dogs.

Telazol® has been implicated in causing nephrosis in lagamorphs (rabbits/hares) and is usually not recommended for use in these species.

Other adverse effects listed by the manufacturer include: emesis during emergence, excessive salivation and bronchial/tracheal secretions (if atropine not administered beforehand), transient apnea, vocalization, erratic and/or prolonged recovery, involuntary muscular twitching, hypertonia, cyanosis, cardiac arrest, pulmonary edema, muscle rigidity, and either hypertension or hypotension.

Reproductive/Nursing Safety

Telazol® crosses the placenta and may cause respiratory depression in newborns; the manufacturer lists its use in cesarean section as being contraindicated. The teratogenic potential of the drug is unknown, and it is not recommended for use during any stage of pregnancy.

Overdosage/Acute Toxicity

The manufacturer claims a 2X margin of safety in dogs, and a 4.5 times margin of safety in cats. A preliminary study in dogs (Hatch et al. 1988) suggests that doxapram at 5.5 mg/kg will enhance respirations and arousal after *Telazol®*. In massive overdoses, it is suggested that mechanically assisted ventilation be performed if necessary and other clinical signs treated symptomatically and supportively.

Drug Interactions

Little specific information is available presently on drug interactions with this product.

- **ANESTHETICS, INHALATIONAL:** Dosage may need to be reduced when used concomitantly with *Telazol®*
- **BARBITURATES:** Dosage may need to be reduced when used concomitantly with *Telazol®*
- **CHLORAMPHENICOL:** In dogs, chloramphenicol apparently has no effect on recovery times with *Telazol®*, but in cats, anesthesia is prolonged on average of 30 minutes by chloramphenicol.
- **PHENOTHIAZINES:** Can cause increased respiratory and cardiac depression

For potential additional interactions from the related compounds, ketamine and midazolam:

Ketamine:

- **NEUROMUSCULAR BLOCKERS** (*e.g.*, **succinylcholine** and **tubocurarine**): May cause enhanced or prolonged respiratory depression
- **THYROID HORMONES:** When given concomitantly with ketamine, thyroid hormones have induced hypertension and tachycardia in humans; beta-blockers (*e.g.*, **propranolol**) may be of benefit in treating these effects

Midazolam:

- **ANESTHETICS, INHALATIONAL:** Midazolam may decrease the dosages required
- **AZOLE ANTIFUNGALS** (**ketoconazole, itraconazole**), **fluconazole**): May increase midazolam levels
- **CALCIUM CHANNEL BLOCKERS** (**diltiazem, verapamil**): May increase midazolam levels
- **CIMETIDINE:** May increase midazolam levels
- **CNS DEPRESSANTS, OTHER:** May increase the risk of respiratory depression
- **MACROLIDES** (**erythromycin, clarithromycin**): May increase midazolam levels
- **OPIATES:** May increase the hypnotic effects of midazolam and hypotension has been reported when used with meperidine.
- **PHENOBARBITAL:** May decrease peak levels and AUC of midazolam
- **RIFAMPIN:** May decrease peak levels and AUC of midazolam
- **THIOPENTAL:** Midazolam may decrease the dosages required

Doses

- **DOGS:**
  a) For diagnostic purposes: 6.6–9.9 mg/kg IM
  For minor procedures of short duration: 9.9–13.2 mg/kg IM; If supplemental doses are necessary, give doses less than the initial dose and total dosage should not exceed 26.4 mg/kg. Atropine 0.04 mg/kg should be used concurrently to control hypersalivation. (Package Insert; *Telazol®*—Robins)
  b) Based upon the combination of drugs: 3–10 mg/kg IM or SC or 2–5 mg/kg IV (Mama 2002a)
- **CATS:**
  a) 9.7–11.9 mg/kg IM for procedures such as dentistry, abscess treatment, foreign body removal, etc. For procedures that require mild to moderate levels of analgesia (lacerations, castration, etc.) use 10.6–12.5 mg/kg IM.
  For ovariohysterectomy and onychectomy use 14.3–15.8 mg/kg IM.
  If supplemental doses are necessary, give doses less than the initial dose and the total dosage should not exceed 72 mg/kg. Atropine 0.04 mg/kg should be used concurrently to control hypersalivation. (Package Insert; *Telazol®*—Robins)
  b) Based upon the combination of drugs: 3–10 mg/kg IM or SC or 2–5 mg/kg IV (Mama 2002a)
- **RUMINANTS:**
  As an induction agent for cattle, llamas/alpacas, goats, sheep:
  a) Xylazine at 0.05–0.1 mg/kg IV, IM, then *Telazol®* at 2–4 mg/kg IV (IM). Caution: xylazine can cause severe hypoxemia and pulmonary edema in sheep. (Haskell 2005a)
- **RABBITS, RODENTS, SMALL MAMMALS:**
  For chemical restraint:
  a) Gerbils: 20 mg/kg IP (in combination with xylazine 10 mg/kg) (Huerkamp 1995)
  b) Mice: 80–100 mg/kg IM.
  Rats: 20–60 mg/kg IM.
  Hamsters/Gerbils: 20–80 mg/kg IM.
  Guinea pig: 10–80 mg/kg IM.
  Rabbits: Not recommended (Burke 1999)
  c) Chinchillas: 20–40 mg/kg IM.
  Hamsters: 50–80 mg/kg IP for immobilization/anesthesia.
  Gerbils: 10–30 mg/kg IP.
  Mice: 80 mg/kg IP for immobilization
  Rats: 40 mg/kg IP for light anesthesia.
  Guinea pigs: 40–60 mg/kg IM for immobilization (Adamcak and Otten 2000)
- **FERRETS:**
  As a sedative/analgesic:
  a) 22 mg/kg IM combined with glycopyrrolate (0.01 mg/kg IM). Rapid onset, but slow and rough recovery (3–4 hours) (Finkler 1999)
  b) *Telazol®* alone: 22 mg/kg IM;
  Telazol® (1.5 mg/kg) plus xylazine (1.5 mg/kg) IM; may reverse xylazine with yohimbine (0.05 mg/kg IM)
  Telazol® (1.5 mg/kg) plus xylazine (1.5 mg/kg) plus butorphanol (0.2 mg/kg) IM; may reverse xylazine with yohimbine (0.05 mg/kg IM) (Williams 2000)
- **HORSES:** (**Note:** ARCI UCGFS Class 2 Drug)
  a) Xylazine 1.1 mg/kg IV, 5 minutes prior to *Telazol®* at 1.65–2.2 mg/kg IV (Hubbell, Bednarski, and Muir 1989)

■ **EXOTIC SPECIES:**

a) An extensive list of suggested *Telazol*® dosages may be found in the article by E. Schobert entitled, "*Telazol*® Use in Wild and Exotic Animals" in the October 1987 issue of Veterinary Medicine.

b) For carnivorous mammals (not tigers): 2–4 mg/mL usually provides adequate restraint. (Suedmeyer 2003)

■ **REPTILES:**

a) Large Snakes: 3 mg/kg IM to facilitate handling and anesthesia. Administer 30–45 minutes prior to handling. Sedation may persist for up to 48 hours. May also be used in Crocodilians at 4–8 mg/kg. (Heard 1999)

b) 3–10 mg/kg IM. Lizards and snakes can generally be treated with lower end of dosage range and chelonians may require high end. If sedation is inadequate, may give incrementally up to the maximum dose. Monitor closely for apnea and ventilate if required. (Innis 2003)

c) Significant interspecies and interpatient differences in effectiveness. At lower doses of 4–10 mg/kg sedation may be sufficient for some procedures (venipuncture, gastric lavage, intubation for inhalation anesthesia). At higher doses (15–40 mg/kg), recovery may be greatly prolonged. Suggest starting out at 7–15 mg/kg the first few times this is used on reptiles in your practice (and to use on your own "in house" pets first!), and then use increasing dosages as needed. (Funk 2002)

■ **BIRDS:**

a) Ratites: 5 mg/kg IM or IV (Jenson 1998)

Monitoring

- Level of anesthesia/analgesia
- Respiratory function; cardiovascular status (rate, rhythm, BP if possible)
- Monitor eyes to prevent drying or injury
- Body temperature

Client Information

Should only be administered by individuals familiar with its use.

Chemistry/Synonyms

Tiletamine is an injectable anesthetic agent chemically related to ketamine. Zolazepam is a diazepinone minor tranquilizer. The pH of the injectable product, after reconstitution, is 2.2–2.8.

Tiletamine HCl may also be known as: CI-634, CL-399, CN-54521-2, or *Telazol*®.

Zolazepam HCl may also be known as: CI-716.

Storage/Stability

After reconstitution, solutions may be stored for 4 days at room temperature and 14 days if refrigerated. Do not use solutions that contain a precipitate or are discolored.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Tiletamine HCl (equivalent to 250 mg free base) and Zolazepam HCl (equivalent to 250 mg free base) as lyophilized powder/vial in 5 mL vials. When 5 mL of sterile diluent (sterile water) is added a concentration of 50 mg/mL of each drug (100 mg/mL combined) is produced; *Telazol*® (Fort Dodge); (Rx, C-III). Approved for use in cats and dogs. *Telazol*® is a Class-III controlled substance.

HUMAN-LABELED PRODUCTS: None

TILMICOSIN

(til-mi-coe-sin) Micotil®, Pulmotil®

MACROLIDE ANTIBIOTIC

Prescriber Highlights

- Macrolide antibiotic used in cattle, sheep, & sometimes rabbits; used in swine as a medicated feed article
- Contraindications: Not to be used in automatically powered syringes or to be given IV
- May be fatal in swine (when injected) & non-human primates; potentially in horses
- Adverse Effects: IM injections may cause a local tissue reaction resulting in trim loss; edema is possible at SC injection site
- Avoid contact with eyes
- In case of human injection, contact physician immediately

Uses/Indications

Tilmicosin is indicated for the treatment of bovine or ovine respiratory diseases (BRD) caused by *Mannheimia* (*Pasturella*) *haemolytica*.

Pharmacology/Actions

Like other macrolides, tilmicosin has activity primarily against gram-positive bacteria, although some gram-negative bacteria are affected and the drug reportedly has some activity against mycoplasma. Preliminary studies have shown that 95% of studied isolates of *Pasturella haemolytica* are sensitive.

Pharmacokinetics

Tilmicosin apparently concentrates in lung tissue. At 3 days post injection, the lung:serum ratio is about 60:1. MIC_{95} concentrations (3.12 micrograms/mL) for *P. Haemolytica* persist for a minimum of 3 days after a single injection.

Contraindications/Precautions/Warnings

Not to be used in automatically powered syringes or to be given intravenously as fatalities may result. Tilmicosin has been shown to be fatal in swine (when injected), non-human primates and potentially, in horses.

Avoid contact with eyes. Accidental self-injection can be fatal in humans. Do not use in automatically powered syringes. Emergency treatment includes applying ice to injection site and contacting a physician immediately. Emergency medical telephone numbers are 1-800-722-0987 or 1-317-276-2000.

Adverse Effects

If administered IM, a local tissue reaction may occur resulting in trim loss. Edema may be noted at the site of subcutaneous injection.

Reproductive/Nursing Safety

Safe use in pregnant animals or animals to be used for breeding purposes has not been demonstrated.