Oxytetracycline may also be known as: glomycin, hydroxytetracycline, oxytetracyclinum, riomitsin, terrafungine, *Biomycin*®, *Liquamycin*®, *Medamycin*®, *Oxyject*®, *Oxytet*®, and *Terramycin*®.

Storage/Stability/Compatibility

Unless otherwise directed by the manufacturer, oxytetracycline HCl and oxytetracycline products should be stored in tight, light-resistant containers at temperatures of less than 40°C (104°F) and preferably at room temperature (15–30°C); avoid freezing.

Oxytetracycline HCl is generally considered to be physically **compatible** with most commonly used IV infusion solutions, including D_5W, sodium chloride 0.9%, and lactated Ringer's, but can become relatively unstable in solutions with a pH >6, particularly in those containing calcium. This is apparently more of a problem with the veterinary injections that are propylene glycol based, rather than those that are povidone based. Other drugs that are reported to be physically **compatible** with oxytetracycline for injection include: colistimethate sodium, corticotropin, dimenhydrinate, insulin (regular), isoproterenol HCl, methyldopate HCl, norepinephrine bitartrate, polymyxin B sulfate, potassium chloride, tetracycline HCl, and vitamin B-complex with C.

Drugs that are reportedly physically **incompatible** with oxytetracycline, data conflicts, or compatibility is concentration/time dependent, include: amikacin sulfate, aminophylline, amphotericin B, calcium chloride/gluconate, carbenicillin disodium, cephalothin sodium, cephapirin sodium, chloramphenicol sodium succinate, erythromycin gluceptate, heparin sodium, hydrocortisone sodium succinate, iron dextran, methicillin sodium, methohexital sodium, oxacillin sodium, penicillin G potassium/sodium, pentobarbital sodium, phenobarbital sodium, and sodium bicarbonate. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status/Withdrawal Times

VETERINARY-LABELED PRODUCTS:

Oxytetracycline HCl 50 mg/mL, 100 mg/mL Injection: There are many approved oxytetracycline products marketed in these concentrations. Some trade names for these products include: *Terramycin*®, *Liquamycin*®, *Biomycin*® (Bio-Ceutic), *Medamycin*® (TechAmerica), *Biocyl*® (Anthony), *Oxyject*® (Fermenta), and *Oxytet*® (BI). Some are labeled for Rx (prescription) use only, while some are over-the-counter (OTC). Depending on the actual product, this drug may be approved for use in swine, cattle, beef cattle, chickens or turkeys. Products may also be labeled for IV, IM, or SC use. Withdrawal times vary with regard to individual products; when used as labeled, slaughter withdrawal times vary in cattle from 15–22 days, swine 20–26 days, and 5 days for chickens and turkeys. Refer to the actual labeled information for the product used for more information.

Oxytetracycline base 200 mg/mL Injection in 100, 250, and 500 mL bottles; *Liquamycin*® *LA-200* (Pfizer); (OTC or Rx). Approved for use in swine and cattle. When used as labeled, slaughter withdrawal = 28 days for swine and cattle; Milk withdrawal = 96 hours

Oxytetracycline Oral Tablets (Boluses) 250 mg tablet; *Terramycin*® *Scours Tablets* (Pfizer); (OTC). Approved for use in non-lactating dairy and beef cattle. Slaughter withdrawal (at labeled doses) = 7 days.

Oxytetracycline is also available in feed additive, premix, ophthalmic, and intramammary products.

Established residue tolerances: Uncooked edible tissues of swine, cattle, salmonids, catfish and lobsters: 0.10 ppm. Uncooked kidneys of chickens or turkeys: 3 ppm. Uncooked muscle, liver, fat or skin of chickens or turkeys: 1 ppm.

HUMAN-LABELED PRODUCTS:

Oxytetracycline For Injection: 50 mg/mL or 125 mg/mL (both with 2% lidocaine) in 2 mL amps and 10 mL multidose vials (125 mg/mL only); *Terramycin*® (Roerig/Pfizer); (Rx)

OXYTOCIN

(ox-i-***toe***-sin) Pitocin®

HORMONAL AGENT

Prescriber Highlights

- Hypothalamic hormone used for induction or enhancement of uterine contractions at parturition, postpartum retained placenta & metritis, uterine involution after manual correction of prolapsed uterus in dogs, & agalactia.
- Contraindications: Known hypersensitivity, dystocia due to abnormal presentation of fetus(es) unless correction is made. When used prepartum, oxytocin should be used only when the cervix is relaxed naturally or by the prior administration of estrogens.
- Treat hypoglycemia or hypocalcemia before using
- Adverse Effects: Usually occur only when used in inappropriate patients or at too high a dosage.
- Drug Interactions

Uses/Indications

In veterinary medicine, oxytocin has been used for induction or enhancement of uterine contractions at parturition, treatment of postpartum retained placenta and metritis, uterine involution after manual correction of prolapsed uterus in dogs, and in treating agalactia.

Pharmacology/Actions

By increasing the sodium permeability of uterine myofibrils, oxytocin stimulates uterine contraction. The threshold for oxytocin-induced uterine contraction is reduced with pregnancy duration, in the presence of high estrogen levels and in patients already in labor.

Oxytocin can facilitate milk ejection, but does not have any galactopoietic properties. While oxytocin only has minimal antidiuretic properties, water intoxication can occur if it is administered at too rapid a rate and/or if excessively large volumes of electrolyte-free intravenous fluids are administered.

Pharmacokinetics

Oxytocin is destroyed in the GI tract and, therefore, must be administered parenterally. After IV administration, uterine response occurs almost immediately. Following IM administration, the uterus responds generally within 3–5 minutes. The duration of effect in dogs after IV or IM/SC administration has been reported to be 13 minutes and 20 minutes, respectively. While oxytocin can be administered intranasally, absorption can be erratic. Oxytocin is distributed throughout the extracellular fluid. It is believed that small quantities of the drug cross the placenta and enter the fetal circulation.

In humans, plasma half-life of oxytocin is about 3–5 minutes. In goats, this value has been reported to be about 22 minutes. Oxytocin is metabolized rapidly in the liver and kidneys and a circulating enzyme, oxytocinase can also destroy the hormone. Very small amounts of oxytocin are excreted in the urine unchanged.

Contraindications/Precautions/Warnings

Oxytocin is considered contraindicated in animals with dystocia due to abnormal presentation of fetus(es), unless correction is made. When used prepartum, oxytocin should be used only when the cervix is relaxed naturally or by the prior administration of estrogens (**Note:** Most clinicians avoid the use of estrogens, as natural relaxation is a better indicator for the proper time to induce contractions.) Oxytocin is also contraindicated in patients who are hypersensitive to it.

Before using oxytocin, treat hypoglycemia or hypocalcemia if present.

In humans, oxytocin is contraindicated in patients with significant cephalopelvic disproportion, unfavorable fetal positions, in obstetrical emergencies when surgical intervention is warranted, severe toxemia, or when vaginal delivery is contraindicated. Nasally administered oxytocin is contraindicated in pregnancy.

Adverse Effects

When used appropriately at reasonable dosages, oxytocin rarely causes significant adverse reactions. Most adverse effects are a result of using the drug in inappropriate individuals (adequate physical exam and monitoring of patient are essential) or at too high doses (see Overdosage below). Most of the older dosage recommendations for dogs or cats are obsolete as mini doses have been found to improve the frequency of uterine contractility, and are less hazardous to the bitch (uterine rupture) and to the fetuses (placental compromise). Hypersensitivity reactions are a possibility in non-synthetically produced products. Repeated bolus injections of oxytocin may cause uterine cramping and discomfort.

Overdosage/Acute Toxicity

Effects of overdosage on the uterus depend on the stage of the uterus and the position of the fetus(es). Hypertonic or tetanic contractions can occur leading to tumultuous labor, uterine rupture, fetal injury, or death.

Water intoxication can occur if large doses are infused for a long period, especially if large volumes of electrolyte-free intravenous fluids are concomitantly being administered. Early clinical signs can include listlessness or depression. More severe intoxication clinical signs can include coma, seizures and eventually death. Treatment for mild water intoxication is stopping oxytocin therapy and restricting water access until resolved. Severe intoxication may require the use of osmotic diuretics (mannitol, urea, dextrose) with or without furosemide.

Reproductive/Nursing Safety

In humans, oxytocin is contraindicated in patients with significant cephalopelvic disproportion, unfavorable fetal positions, in obstetrical emergencies when surgical intervention is warranted, severe toxemia, or when vaginal delivery is contraindicated. Nasally administered oxytocin is contraindicated in pregnancy.

No known indications for use in the first trimester exist other than in relation to spontaneous or induced abortion. Oxytocin is not expected to present a risk of fetal abnormalities when use as indicated.

Oxytocin may be found in small quantities in maternal milk but is unlikely to have significant effects.

Drug Interactions

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

- **THIOPENTAL:** One case in humans has been reported where thiopental anesthesia was delayed when oxytocin was being administered. The clinical significance of this interaction has not been firmly established.
- **VASOCONSTRICTORS:** If sympathomimetic agents or other vasoconstrictors are used concurrently with oxytocin post-partum hypertension may result. Monitor and treat if necessary.

Doses

- **DOGS:**

  To augment uterine contractions during parturition:

  a) 0.5–3 Units SC or IM every 30–60 minutes, best based upon the results of tokodynamometry. (Davidson 2004b)

  For uterine inertia if no fetuses in birth canal, cervix is dilated, and fetal and maternal obstruction have been ruled out:

  a) Oxytocin at 5–20 Units (depending on size of animal) IM or as an IV drip (10 Units/liter) beginning as a slow drip and gradually increasing until effective contractions are observed. If no response to IM injection in 30 minutes, may repeat along with 10% dextrose IV slowly. If no response again in 30 minutes, repeat IM again. Some texts recommend giving calcium gluconate (2–10 mL slowly IV while monitoring ECG for bradycardia or arrhythmias). If no response to this medical management, perform Caesarian section. (Macintire 2006e)

  To induce milk let-down in bitches with adequate milk production and who tolerate nursing:

  a) Oxytocin nasal spray (*Syntocinon®*): 5–10 minutes prior to nursing three times daily (Loar 1988)

  For adjunctive treatment of acute metritis:

  a) To promote uterine involution and evacuation: 0.5–1 Unit/kg IM; may repeat in 1–2 hours. It's less effective if parturition occurred several days ago. (Magne 1986)

  To promote uterine involution after uterine prolapse manual reduction:

  a) 5–20 Units IM (Nelson 1988)

- **CATS:**

  To promote uterine involution after uterine prolapse manual reduction:

  a) 5 Units IM once (Morgan 1988)

  To treat primary uterine inertia:

  a) 0.25–1 unit SC or IM every 30–60 minutes, best based upon the results of tokodynamometry (Davidson 2004b)

- **RABBITS, RODENTS, SMALL MAMMALS:**

  a) Mice, Rats, Gerbils, Hamsters, Guinea pigs, Chinchillas: 0.2–3 IU/kg IV, IM or SC (Adamcak and Otten 2000)

- **CATTLE:**

  For retained placenta in patients

  a) 40–60 Units oxytocin q2h (often used in conjunction with intravenous calcium therapy) as necessary. Of limited value after 48 hours postpartum as uterine sensitivity is reduced. (McClary 1986)

  b) To reduce incidence of retained placenta: 20 Units IM immediately following calving and repeated 2–4 hours later (Hameida, Gustafsson, and Whitmore 1986)

  For mild to moderate cases of acute post-partum metritis:

  a) 20 Units IM 3–4 times a day for 2–3 days (Hameida, Gustafsson, and Whitmore 1986)

To augment uterine contractions during parturition:
a) 30 Units IM; repeat no sooner than 30 minutes if necessary (Wheaton 1989)
b) For obstetrical use in cows: 100 Units IV, IM or SC (Package Insert; Oxytocin Injection—Anthony Products)

For milk let-down in cows:
a) 10–20 Units IV (Package Insert; Oxytocin Injection—Anthony Products)

■ **HORSES:**

To augment or initiate uterine contractions during parturition in properly evaluated mares:
a) For induction: 2.5–5 IU IV, every 15–20 minutes until foal is born (McCue 2003a)

For evacuation of uterine fluid:
a) 20 IU IV or IM one to three times a day (McCue 2003a)

To aid in removal of retained fetal membranes:
a) Oxytocin: 30–100 Units in 1 liter of normal saline IV over 30–60 minutes *or* 10–120 IU IM *or* 10–40 IU by IV bolus (**Note:** large dose IV boluses are not recommended as they may cause uterine spasm and abdominal discomfort) (Perkins 1999)
b) Oxytocin: 20 IU IV or IM given every hour beginning 2–3 hours after foaling. Repeat as needed. (McCue 2003a)

For mild to moderate cases of acute post-partum metritis:
a) 20 Units IM 3–4 times a day for 2–3 days (Hameida, Gustafsson, and Whitmore 1986)

■ **SWINE:**

For adjunctive treatment of agalactia syndrome (MMA) in sows:
a) 30–40 Units per sow at 3–4 hours (Powe 1986)
b) 20–50 Units IM or 5–10 Units IV (Einarsson 1986)

For retained placenta in patients with uterine atony:
a) 20–30 Units oxytocin q2–3h as necessary (with broad-spectrum antibiotics) (McClary 1986)

To augment uterine contractions during parturition:
a) 10 Units IM; repeat no sooner than 30 minutes if necessary (Wheaton 1989)
b) For obstetrical use in sows: 30–50 Units IV, IM or SC (Package Insert; Oxytocin Injection—Anthony Products)

For mild to moderate cases of acute post-partum metritis:
a) 5–10 Units IM 3–4 times a day for 2–3 days (Hameida, Gustafsson, and Whitmore 1986)
b) 5 Units IM; may need to be repeated as effect may be as short as 30 minutes (Meredith 1986)

For milk let-down in sows:
a) 5–20 Units IV (Package Insert; Oxytocin Injection—Anthony Products)

■ **SHEEP & GOATS:**

For retained placenta in patients with uterine atony:
a) 10–20 Units oxytocin. Of limited value after 48 hours postpartum as uterine sensitivity is reduced. If signs of metritis develop, treat with antibiotics. (McClary 1986)

For mild to moderate cases of acute post-partum metritis:
a) 5–10 Units IM 3–4 times a day for 2–3 days (Hameida, Gustafsson, and Whitmore 1986)

To control post-extraction cervical and uterine bleeding after internal manipulations (*e.g.,* fetotomy, etc.):
a) Goats: 10–20 Units IV, may repeat SC in 2 hours (Franklin 1986a)

■ **BIRDS:**

As a uterotonic agent:
a) 0.5 IU/kg IM; may repeat in 60 minutes (Pollock 2007b)

For egg expulsion:
a) 0.01–0.1 mL once IM. Should be administered with Vitamin A and calcium (injectable) (Clubb 1986)

■ **REPTILES:**

For egg binding in combination with calcium (Calcium glubionate:
a) Calcium glubionate (10–50 mg/kg IM as needed until calcium levels back to normal or egg binding is resolved); oxytocin: 1–10 IU/kg IM. Use care when giving multiple injections. Not as effective in lizards as in other species. (Gauvin 1993)

To induce oviposition:
a) Doses range from 1–30 IU/kg. A dose of 10 IU/kg appears to be effective in many chelonians. May have to repeat in several hours, but there is a risk of oviduct rupture if cloaca is obstructed or eggs cannot pass for other reasons. (Lewbart 2001)

Monitoring

■ Uterine contractions, status of cervix
■ Fetal monitoring if available and indicated

Client Information

■ Oxytocin should only be used by individuals able to adequately monitor its effects.

Chemistry/Synonyms

A nonapeptide hypothalamic hormone stored in the posterior pituitary (in mammals), oxytocin occurs as a white powder that is soluble in water. The commercially available preparations are highly purified and have virtually no antidiuretic or vasopressor activity when administered at usual doses. Oxytocin potency is standardized according to its vasopressor activity in chickens and is expressed in USP Posterior Pituitary Units. One unit is equivalent of approximately 2–2.2 micrograms of pure hormone.

Commercial preparations of oxytocin injection have their pH adjusted with acetic acid to 2.5–4.5 and multi-dose vials generally contain chlorobutanol 0.5% as a preservative.

Oxytocin may also be known as: alpha-hypophamine, or oxytocinum and *Pitocin*®.

Storage/Stability/Compatibility

Oxytocin injection should be stored at temperatures of less than 25°C, but should not be frozen. Some manufacturers recommend storing the product under refrigeration (2–8°C), but some products have been demonstrated to be stable for up to 5 years if stored at less than 26°C.

Oxytocin is reportedly physically **compatible** with most commonly used intravenous fluids and the following drugs: chloramphenicol sodium succinate, metaraminol bitartrate, netilmicin sulfate, sodium bicarbonate, tetracycline HCl, thiopental sodium, and verapamil HCl.

Oxytocin is reportedly physically **incompatible** with the following drugs: fibrinolysin, norepinephrine bitartrate, prochlorperazine edisylate, and warfarin sodium. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Oxytocin for Injection: 20 USP Units/mL in 10 mL, 30 mL, and 100 mL vials; available labeled generically from several manufacturers; (Rx). Oxytocin products are labeled for several species, including horses, dairy cattle, beef cattle, sheep, swine, cats, and dogs. There are no milk or meat withdrawal times specified for oxytocin.

HUMAN-LABELED PRODUCTS:

Oxytocin for Injection: 10 Units/mL in 1 mL amps, 3 mL and 10 mL vials; 1 mL *Steri-Dose* syringes and 1 mL *Steri-Vials*; *Pitocin*® (Monarch); generic; (Rx)

PAMIDRONATE DISODIUM

(pah-*mih*-dro-nate) Aredia®

BISPHOSPHONATE

Prescriber Highlights

- Bisphosphonate used IV for treating hypercalcemia associated with Vitamin D-analog toxicity or hypercalcemia of malignancy; being investigated for adjuvant treatment of osteosarcomas
- Must be given IV in saline over several hours
- Potentially can cause electrolyte abnormalities, anemias, or renal toxicity
- Expense may be an issue

Uses/Indications

Pamidronate may be useful in treating hypercalcemia associated with vitamin D-related toxicoses or hypercalcemia of malignancy. There is ongoing research on the use of this drug to determine if it has clinical usefulness in directly treating "micro-metastases" in osteosarcomas.

Pharmacology/Actions

Bisphosphonates at therapeutic levels inhibit bone resorption and do not inhibit bone mineralization via binding to hydroxyapatite crystals. They impede osteoclast activity, and induce osteoclast apoptosis. Pamidronate has approximately 100 times greater relative antiresorptive potency when compared to etidronate.

Bisphosphonates *in vitro* have direct cytotoxic or cytostatic effects on human osteosarcoma cell lines. They may also have antiangiogenic effects and inhibit cell migration in certain cancers.

Pharmacokinetics

After intravenous infusion in rats, 50–60% of the dose is rapidly absorbed by bone. Bone uptake is highest in areas of rapid bone turnover. The kidneys very slowly eliminate the drug. Terminal half-life is on the order of 300 days in rats.

Contraindications/Precautions/Warnings

Pamidronate is contraindicated in patients hypersensitive to it or any of the bisphosphonate drugs. It should be used with caution in patients with impaired renal function; the drug has been associated with renal toxicity. In humans, it has not been tested in patients with serum creatinine levels greater than 5 mg/dl.

Adverse Effects

Electrolyte abnormalities may occur with pamidronate therapy. One case of a dog developing hypomagnesemia and arrhythmias after pamidronate has been reported (Kadar, Rush et al. 2004). Pamidronate may cause renal toxicity in dogs, but it is thought this can be minimized or avoided by infusing the drug over at least 2 hours. Anemia, thrombocytopenia and granulocytosis have been reported in humans.

Reproductive/Nursing Safety

In pregnant humans, the FDA as a category ***D*** drug (*There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.*) Pamidronate has produced both maternal and embryo/fetal toxicity in laboratory animals when given at dosages therapeutically used in human patients. If it is used in pregnant veterinary patients, informed consent by the owner accepting the risks to both mother and offspring is recommended.

It is unknown if pamidronate is excreted into milk. Use with caution in nursing mothers.

Overdosage/Acute Toxicity

Overdosage of pamidronate may cause hypocalcemia, including tetany. Should this occur, treat with short-term, intravenous calcium.

Drug Interactions

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

- **CALCIUM-AFFECTING DRUGS** (*e.g.*, **furosemide**, **corticosteroids**): Pamidronate must be used carefully (with monitoring) when used in conjunction with other drugs that can affect calcium
- **NEPHROTOXIC DRUGS** (*e.g.*, **cisplatin, aminoglycosides**): Use with caution, potential for increased risk for nephrotoxicity

Laboratory Considerations

No specific laboratory interactions or considerations noted.

Doses

- **DOGS:**
  a) For refractory hypercalcemia: 1 mg/kg IV given over 2 hours in 250 mL of normal saline every 4 weeks. (Chun 2007c)
  b) For control of hypercalcemia: Treat each patient individually and if possible remove the underlying cause. If parenteral saline, furosemide and corticosteroids do not resolve the issue then bisphosphonates can be considered for more chronic control of hypercalcemia. Pamidronate 1.3–2 mg/kg in 150 mL of 0.9% saline with a 2 hour IV infusion; can repeat in 1–3 weeks. (Chew, Schenck et al. 2003)
  c) For treatment of cholecalciferol-induced toxicosis: 0.65–2 mg/kg in 0.9% NaCl on days 1 and 4 post-ingestion (Rumbeiha, Fitzgerald et al. 2000)
  d) For attempting to reduce bone pain associated with osteosarcoma in combination with an NSAID: 1–2 mg/kg; diluted into 250 mL of 0.9% sodium chloride and administered as a CRI over 2 hours every 28 days. (Fan and de Lorimier 2003), (Fan, de Lorimier et al. 2007)
  e) For calcipotriene toxicosis: 1.3–2 mg/kg slow IV infusion. In most cases, a single dose will lower calcium levels back to normal levels. Recommended to monitor calcium levels daily for at least 10 days after they have returned to normal. (Gwaltney-Brant 2003)
- **CATS:**
  a) For control of hypercalcemia: 1.5–2 mg/kg IV (from a retrospective study of 2 cats). (Hostutler, Chew et al. 2005)