Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 1 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Oxymorphone HCl Tablets: 5 mg & 10 mg; *Opana®* (Endo Pharmaceuticals); (Rx, C-II)

Oxymorphone HCl Extended-Release Tablets: 5 mg, 10 mg, 20 mg & 40 mg; *Opana® ER* (Endo Pharmaceuticals); (Rx, C-II)

Oxymorphone HCl for Injection: 1 mg/mL in 1 mL amps; *Numorphan®* (Endo Laboratories); (Rx, C-II)

Note: Oxymorphone is a Class-II controlled substance. Very accurate record keeping is required as to use and disposition of stock.

OXYTETRACYCLINE
OXYTETRACYCLINE HCL

(ox-it-tet-ra-**sye**-kleen) Terramycin®

TETRACYCLINE ANTIBIOTIC

Prescriber Highlights

- Tetracycline antibiotic; while many bacteria are now resistant, it still may be very useful to treat mycoplasma, rickettsia, spirochetes, & Chlamydia
- Contraindications: Hypersensitivity. Extreme Caution: Pregnancy. Caution: Liver, renal insufficiency
- Adverse Effects: GI distress, staining of developing teeth & bones, superinfections, photosensitivity; long-term use may cause uroliths. CATS do not tolerate very well. HORSES: if stressed may break with diarrheas (oral use). RUMINANTS: high oral doses can cause ruminal microflora depression & ruminoreticular stasis. Rapid IV of undiluted propylene glycol-based products can cause intravascular hemolysis & cardiodepressant effects. IM: local reactions, yellow staining & necrosis may be seen at the injection site.

Uses/Indications

Oxytetracycline products are approved for use in dogs and cats (no known products are being marketed, however), calves, non-lactating dairy cattle, beef cattle, swine, fish, and poultry. For more information, refer to the Doses section, below.

Pharmacology/Actions

Tetracyclines generally act as bacteriostatic antibiotics and inhibit protein synthesis by reversibly binding to 30S ribosomal subunits of susceptible organisms, preventing binding to those ribosomes of aminoacyl transfer-RNA. Tetracyclines also are believed to reversibly bind to 50S ribosomes and additionally alter cytoplasmic membrane permeability in susceptible organisms. In high concentrations, tetracyclines can also inhibit protein synthesis by mammalian cells.

As a class, the tetracyclines have activity against most mycoplasma, spirochetes (including the Lyme disease organism), Chlamydia, and Rickettsia. Against gram-positive bacteria, the tetracyclines have activity against some strains of staphylococci and streptococci, but resistance of these organisms is increasing. Gram-positive bacteria that are usually covered by tetracyclines, include *Actinomyces* spp. , *Bacillus anthracis, Clostridium perfringens* and *tetani*, *Listeria monocytogenes*, and Nocardia. Among gram-negative bacteria that tetracyclines usually have *in vitro* and *in vivo* activity include *Bordetella* spp. , Brucella, Bartonella, *Haemophilus* spp., *Pasturella multocida,* Shigella, and *Yersinia pestis*. Many or most strains of *E. coli,* Klebsiella, Bacteroides, Enterobacter, Proteus and *Pseudomonas aeruginosa* are resistant to the tetracyclines. While most strains of *Pseudomonas aeruginosa* show *in vitro* resistance to tetracyclines, those compounds attaining high urine levels (*e.g.*, tetracycline, oxytetracycline) have been associated with clinical cures in dogs with UTI secondary to this organism.

Oxytetracycline and tetracycline share nearly identical spectrums of activity and patterns of cross-resistance. A tetracycline susceptibility disk is usually used for *in vitro* testing for oxytetracycline susceptibility.

Pharmacokinetics

Both oxytetracycline and tetracycline are readily absorbed after oral administration to fasting animals. Bioavailabilities are approximately 60–80%. The presence of food or dairy products can significantly reduce the amount of tetracycline absorbed, with reductions of 50% or more possible. After IM administration of oxytetracycline (not long-acting), peak levels may occur in 30 minutes to several hours, depending on the volume and site of injection. The long-acting product (*LA-200®*) has significantly slower absorption after IM injection.

Tetracyclines as a class are widely distributed in the body, including to the heart, kidney, lungs, muscle, pleural fluid, bronchial secretions, sputum, bile, saliva, urine, synovial fluid, ascitic fluid, and aqueous and vitreous humor. Only small quantities of tetracycline and oxytetracycline are distributed to the CSF and therapeutic levels may not be attainable. While all tetracyclines distribute to the prostate and eye, doxycycline or minocycline penetrate better into these and most other tissues. Tetracyclines cross the placenta, enter fetal circulation and are distributed into milk. The volume of distribution of oxytetracycline is approximately 2.1 L/kg in small animals, 1.4 L/kg in horses, and 0.8 L/kg in cattle. The amount of plasma protein binding is about 10–40% for oxytetracycline.

Both oxytetracycline and tetracycline are eliminated unchanged primarily via glomerular filtration. Patients with impaired renal function can have prolonged elimination half-lives and may accumulate the drug with repeated dosing. These drugs apparently are not metabolized, but are excreted into the GI tract via both biliary and nonbiliary routes and may become inactive after chelation with fecal materials. The elimination half-life of oxytetracycline is approximately 4–6 hours in dogs and cats, 4.3–9.7 hours in cattle, 10.5 hours in horses, 6.7 hours in swine, and 3.6 hours in sheep.

Contraindications/Precautions/Warnings

Oxytetracycline is contraindicated in patients hypersensitive to it or other tetracyclines. Because tetracyclines can retard fetal skeletal development and discolor deciduous teeth, they should only be used in the last half of pregnancy when the benefits outweigh the fetal risks. Oxytetracycline and tetracycline are considered more likely to cause these abnormalities than either doxycycline or minocycline.

In patients with renal insufficiency or hepatic impairment, oxytetracycline and tetracycline must be used cautiously. Lower than normal dosages are recommended with enhanced monitoring of renal and hepatic function. Avoid concurrent administration of other nephrotoxic or hepatotoxic drugs with tetracyclines. Monitoring of serum levels should be considered if long-term therapy is required.

Adverse Effects

Oxytetracycline and tetracycline given to young animals can cause a yellow, brown, or gray discoloration of bones and teeth. High dosages or chronic administration may delay bone growth and healing.

Tetracyclines in high levels can exert an antianabolic effect, which can cause an increase in BUN and/or hepatotoxicity, particularly in patients with preexisting renal dysfunction. As renal function deteriorates secondary to drug accumulation, this effect may be exacerbated.

In ruminants, high oral doses can cause ruminal microflora depression and ruminoreticular stasis. Rapid intravenous injection of undiluted propylene glycol-based products can cause intravascular hemolysis with resultant hemoglobinuria. Propylene glycol based products have also caused cardiodepressant effects when administered to calves. When administered IM, local reactions, yellow staining, and necrosis may be seen at the injection site.

In small animals, tetracyclines can cause nausea, vomiting, anorexia, and diarrhea. Cats do not tolerate oral tetracycline or oxytetracycline very well, and may present with clinical signs of colic, fever, hair loss, and depression. There are reports that long-term tetracycline use may cause urolith formation in dogs.

Horses, who are stressed by surgery, anesthesia, trauma, etc., may break with severe diarrheas after receiving tetracyclines (especially with oral administration).

Tetracycline therapy (especially long-term) may result in overgrowth (superinfections) of non-susceptible bacteria or fungi.

Tetracyclines have also been associated with photosensitivity reactions and, rarely, hepatotoxicity or blood dyscrasias.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***D*** for use during pregnancy (*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.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as class: ***D*** (*Contraindicated. These drugs have been shown to cause congenital malformations or embryotoxicity.*)

Tetracyclines are excreted in maternal milk. Milk to plasma ratios varies between 0.25 to 1.5. Because of the potential for serious adverse reactions, decide whether to discontinue nursing or discontinue the drug.

Overdosage/Acute Toxicity

Tetracyclines are generally well tolerated after acute overdoses. Dogs given more than 400 mg/kg/day orally or 100 mg/kg/day IM of oxytetracycline did not demonstrate any toxicity. Oral overdoses would most likely be associated with GI disturbances (vomiting, anorexia, and/or diarrhea). Should the patient develop severe emesis or diarrhea, fluids and electrolytes should be monitored and replaced if necessary. Chronic overdoses may lead to drug accumulation and nephrotoxicity.

High oral doses given to ruminants, can cause ruminal microflora depression and ruminoreticular stasis. Rapid intravenous injection of undiluted propylene glycol-based products can cause intravascular hemolysis with resultant hemoglobinuria.

Rapid intravenous injection of tetracyclines has induced transient collapse and cardiac arrhythmias in several species, presumably due to chelation with intravascular calcium ions. Overdose quantities of drug could exacerbate this effect if given too rapidly IV. If the drug must be given rapidly IV (less than 5 minutes), some clinicians recommend pre-treating the animal with intravenous calcium gluconate.

Drug Interactions

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

- **ATOVAQUONE:** Tetracyclines have caused decreased atovaquone levels
- **BETA-LACTAM** or **AMINOGLYCOSIDE ANTIBIOTICS:** Bacteriostatic drugs, like the tetracyclines, may interfere with bactericidal activity of the penicillins, cephalosporins, and aminoglycosides; there is some controversy regarding the actual clinical significance of this interaction, however.
- **DIGOXIN:** Tetracyclines may increase the bioavailability of digoxin in a small percentage of human patients and lead to digoxin toxicity. These effects may persist for months after discontinuation of the tetracycline.
- **DIVALENT OR TRIVALENT CATIONS** (**oral antacids, saline cathartics or other GI products containing aluminum, calcium, iron, magnesium, zinc, or bismuth cations**): When orally administered, tetracyclines can chelate divalent or trivalent cations that can decrease the absorption of the tetracycline or the other drug if it contains these cations; it is recommended that all oral tetracyclines be given at least 1–2 hours before or after the cation-containing products.
- **METHOXYFLURANE:** Fatal nephrotoxicity has occurred in humans when used with tetracycline; concomitant use with oxytetracycline is not recommended
- **WARFARIN:** Tetracyclines may depress plasma prothrombin activity and patients on anticoagulant) therapy may need dosage adjustment

Laboratory Considerations

- Tetracyclines (not minocycline) may cause falsely elevated values of **urine catecholamines** when using fluorometric methods of determination.
- Tetracyclines reportedly can cause false-positive **urine glucose** results if using the cupric sulfate method of determination (Benedict's reagent, *Clinitest*®), but this may be the result of ascorbic acid, which is found in some parenteral formulations of tetracyclines. Tetracyclines have also reportedly caused false-negative results in determining urine glucose when using the glucose oxidase method (*Clinistix*®, *Tes-Tape*®).

Doses

- **DOGS:**

  For susceptible infections:
  a) For systemic infections: 22 mg/kg PO q8h for 7–14 days or 20 mg/kg IM (using repositol form) every 7 days as needed. (Greene, Hartmannn et al. 2006)
  b) 20 mg/kg PO q8–12h; (may give with food if GI upset occurs; avoid or reduce dose in animals with renal or severe liver failure; avoid in young, pregnant or breeding animals) (Vaden and Papich 1995)

- **CATS:**

  For susceptible infections:
  a) For hemotropic mycoplasmosis: 10–25 mg/kg PO, IV q8h for 5–7 days (Greene, Hartmannn et al. 2006)
  b) 20 mg/kg PO q8–12h; (may give with food if GI upset occurs; avoid or reduce dose in animals with renal or severe liver failure; avoid in young, pregnant or breeding animals) (Vaden and Papich 1995)
  c) For haemobartonellosis: 16–20 mg/kg PO three times daily for 3 weeks (Lissman 1988)

■ **RABBITS, RODENTS, SMALL MAMMALS:**

a) Rabbits: 15–50 mg/kg SC, IM q8h; 15–50 mg/kg PO once daily; 1 mg/mL in drinking water (Ivey and Morrisey 2000)

b) Chinchillas: 50 mg/kg PO q12h (Hayes 2000); (Adamcak and Otten 2000)

c) Gerbils: 10 mg/kg PO q8h or 20 mg/kg SC q24h; Guinea Pigs: 50 mg/kg, PO q12h; Hamsters: 16 mg/kg, SC q24h; Mice: 10–20 mg/kg PO q8h; Rats: 10–20 mg/kg PO q8h or 6–10 mg/kg IM q12h (Adamcak and Otten 2000)

■ **CATTLE:**

For susceptible infections:

a) 5–10 mg/kg IM q24h or 20 mg/kg q48–72h IM if depot form (*LA®-200*); 2.5–5 mg/kg, IV q24h; 10–20 mg/kg, PO q12h (Jenkins 1986)

b) For respiratory tract infections: Using 50 mg/mL product: 11 mg/kg IM or SC q24h or IV q12–24h;

Using 100 mg/mL, product: 20 mg/kg IM q24h;

Using 200 mg/mL, product (*LA-200®*): 20 mg/kg IM q3–4 days;

IM or SC doses should be injected into the neck and not more than 10 mL per site. IM route may lead to myositis and abscesses. Rapid IV injection may cause collapse. Phlebitis is possible with IV dosing. (Beech 1987b)

c) For anthrax: 4.4 mg/kg IM or IV daily. Do not use in healthy animals recently vaccinated against anthrax as the protective effect of the vaccine may be negated. (Kaufmann 1986)

d) For bovine anaplasmosis:

For control: At start of vector season give 6.6–11 mg/kg (if using 50 mg/mL or 100 mg/mL product) or 20 mg/kg (if using depot form —*LA®-200*) every 21–28 days and extending 1–2 months after vector season ends.

To eliminate carrier state: If using 50 mg/mL or 100 mg/mL product: 22 mg/kg IM (not over 10 mL per injection site) or IV (diluted in saline) daily for 5 days; or 11 mg/kg as above for 10 days. If using depot form (*LA®-200*): Give 20 mg/kg for 4 treatments deep IM in two separate injection sites at 3-day intervals.

For treatment of sick animals: Preferably using depot form (*LA®-200*): Give 20 mg/kg one time.

For temporary/prolonged protection for rest of herd: If using 50 mg/mL or 100 mg/mL product: 6.6–11 mg/kg IM (not over 10 mL per injection site) repeat at 21–28 day intervals throughout vector season for prolonged protection. If using depot form (*LA®-200*): Give 20 mg/kg IM as above and repeat at 28-day intervals for prolonged protection. (Richey 1986)

e) For pneumonia: If using 50 mg/mL or 100 mg/mL product: 11 mg/kg SC once daily. If using depot form (*LA®-200*): Give 20 mg/kg IM q48h (Hjerpe 1986)

■ **HORSES:**

For susceptible infections:

a) Foals: 5–10 mg/kg IV q12h diluted and given slowly, or 10–20 mg/kg IV q24h diluted and given slowly. Monitor creatinine and UA. (Bentz 2007)

b) Drug of choice for equine monocytic or granulocytic ehrlichiosis: 6.6 mg/kg IV q24h; to safeguard against adverse effects (muscle tremors, agitation or acute collapse) dilute at least in a 1:1 ratio and give IV slowly, or deliver it as an infusion in 500 mL or 1 liter of fluids. (Bentz 2007)

c) For Lyme disease: 6.6 mg/kg IV once to twice daily (Divers 1999)

d) For Potomac Horse Fever (*Ehrlichia risticii*) early in the clinical course of the disease: 6.6 mg/kg IV twice a day. Usually no more than 5 days treatment is necessary.

For Equine Granulocytic Ehrlichiosis: 7 mg/kg once daily for 5–7 days (Madigan and Pusterla 2000)

e) For intrauterine infusion: 1–5 grams; use povidone based products only. Little science is available for recommending doses, volume infused, frequency, diluents, etc. Most intrauterine treatments are commonly performed every day or every other day for 3–7 days. (Perkins 1999)

■ **SWINE:**

For susceptible infections:

a) For anthrax: 4.4 mg/kg IM or IV daily. Do not use in healthy animals recently vaccinated against anthrax as the protective effect of the vaccine may be negated. (Kaufmann 1986)

b) 6–11 mg/kg IV or IM; 10–20 mg/kg PO q6h (Howard 1986)

c) If using 50 mg/mL or 100 mg/mL product: 10 mg/kg IM initially, then 7.5 mg/kg IM once daily (Baggot 1983)

■ **SHEEP & GOATS:**

For susceptible infections:

a) For anthrax: 4.4 mg/kg IM or IV daily. Do not use in healthy animals recently vaccinated against anthrax as the protective effect of the vaccine may be negated. (Kaufmann 1986)

b) 6–11 mg/kg IV or IM; 10–20 mg/kg PO q6h (Howard 1986)

■ **BIRDS:**

For chlamydiosis (Psittacosis):

a) Using 200 mg/mL product (*LA-200®*): 50 mg/kg IM once every 3–5 days in birds suspected or confirmed of having disease. Used in conjunction with other forms of tetracyclines. IM injections may cause severe local tissue reactions. (McDonald 1989)

b) Using 200 mg/mL, product (*LA-200®*): 200 mg/kg IM once daily for 3–5 days. Has worked well in treating breeding birds to control outbreak and while getting birds to eat oral forms doxycycline or chlortetracycline. (Clubb 1986)

■ **REPTILES:**

For susceptible infections:

a) For turtles and tortoises: 10 mg/kg PO once daily for 7 days (useful in ulcerative stomatitis caused by Vibrio) (Gauvin 1993)

Monitoring

■ Adverse effects

■ Clinical efficacy

■ Long-term use or in susceptible patients: periodic renal, hepatic, hematologic evaluations

Client Information

■ Avoid giving this drug orally within 1–2 hours of feeding, milk, or other dairy products

Chemistry/Synonyms

A tetracycline derivative obtained from *Streptomyces rimosus*, oxytetracycline base occurs as a pale yellow to tan, crystalline powder that is very slightly soluble in water and sparingly soluble in alcohol. Oxytetracycline HCl occurs as a bitter-tasting, hygroscopic, yellow, crystalline powder that is freely soluble in water and sparingly soluble in alcohol. Commercially available 50 mg/mL and 100 mg/mL oxytetracycline HCl injections are usually available in either propylene glycol or povidone-based products.

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.