

## TETRACYCLINES Veterinary—Systemic

This monograph includes information on the following: Chlortetracycline; Doxycycline; Oxytetracycline; Tetracycline.

Some commonly used *brand names* are:

For veterinary-labeled products—

<i>Agrimycin 100</i> [Oxytetracycline]	<i>Oxytet-250 Concentrate</i> [Oxytetracycline]
<i>Agrimycin 200</i> [Oxytetracycline]	<i>Oxytetra -A</i> [Oxytetracycline]
<i>Agrimycin -343</i> [Oxytetracycline]	<i>Oxytetracycline 50</i> [Oxytetracycline]
<i>Alamycin LA</i> [Oxytetracycline]	<i>Oxytetracycline 100</i> [Oxytetracycline]
<i>AmTech Chlortetracycline HCL Soluble Powder</i> [Chlortetracycline]	<i>Oxytetracycline 200</i> [Oxytetracycline]
<i>AmTech Maxim-100</i> [Oxytetracycline]	<i>Oxytetracycline 100LP</i> [Oxytetracycline]
<i>AmTech Maxim-200</i> [Oxytetracycline]	<i>Oxy Tetra Forte</i> [Oxytetracycline]
	<i>Oxytetracycline 100</i> [Oxytetracycline]
<i>AmTech Oxytetracycline HCL Soluble Powder</i> [Oxytetracycline]	<i>Oxytet-25-S</i> [Oxytetracycline]
<i>AmTech Oxytetracycline HCL Soluble Powder-343</i> [Oxytetracycline]	<i>Oxytet Soluble</i> [Oxytetracycline]
<i>AmTech Tetracycline Hydrochloride Soluble Powder-324</i> [Tetracycline]	<i>Oxytet-SP</i> [Oxytetracycline]
<i>Aureomycin 110G</i> [Chlortetracycline]	<i>Oxytet-343 Water Soluble Powder</i> [Oxytetracycline]
<i>Aureomycin 220G</i> [Chlortetracycline]	<i>Oxyvet 200 LA</i> [Oxytetracycline]
<i>Aureomycin 50 Granular</i> [Chlortetracycline]	<i>Oxyvet 100 LP</i> [Oxytetracycline]
<i>Aureomycin 90 Granular</i> [Chlortetracycline]	<i>Panmycin Aquadrops</i> [Tetracycline]
<i>Aureomycin 100 Granular</i> [Chlortetracycline]	<i>Pennchlor 50•G</i> [Chlortetracycline]
<i>Aureomycin Soluble Powder</i> [Chlortetracycline]	<i>Pennchlor 90•G</i> [Chlortetracycline]
<i>Aureomycin Soluble Powder Concentrate</i> [Chlortetracycline]	<i>Pennchlor 100 Hi-Flo Meal</i> [Chlortetracycline]
<i>Aureomycin Uterine Oblets</i> [Chlortetracycline]	<i>Pennchlor 50 Meal</i> [Chlortetracycline]
<i>Biomycin 200</i> [Oxytetracycline]	<i>Pennchlor 70 Meal</i> [Chlortetracycline]
<i>Calf Scour Bolus Antibiotic</i> [Tetracycline]	<i>Pennchlor 100 MR</i> [Chlortetracycline]
<i>Chlor 50</i> [Chlortetracycline]	<i>Pennchlor 64 Soluble Powder</i> [Chlortetracycline]
<i>Chlor 100</i> [Chlortetracycline]	<i>Pennox 100 Hi-Flo Meal</i> [Oxytetracycline]
<i>ChlorMax 50</i> [Chlortetracycline]	<i>Pennox 200 Hi-Flo Meal</i> [Oxytetracycline]
<i>Chlorosol-50</i> [Chlortetracycline]	<i>Pennox 200 Injectable</i> [Oxytetracycline]
<i>CLTC 100 MR</i> [Chlortetracycline]	<i>Pennox 50 Meal</i> [Oxytetracycline]
<i>CTC 50</i> [Chlortetracycline]	<i>Pennox 100-MR</i> [Oxytetracycline]
<i>CTC Soluble Powder Concentrate</i> [Chlortetracycline]	<i>Pennox 343 Soluble Powder</i> [Oxytetracycline]
<i>Duramycin 10</i> [Tetracycline]	<i>PolyOtic Soluble Powder</i> [Tetracycline]
<i>Duramycin 72-200</i> [Oxytetracycline]	<i>Promycin 100</i> [Oxytetracycline]
<i>Duramycin 100</i> [Oxytetracycline]	<i>Solu -Tet</i> [Tetracycline]
<i>Duramycin -324</i> [Tetracycline]	<i>Solu -Tet 324</i> [Tetracycline]
<i>Foul Brood Mix</i> [Oxytetracycline]	<i>Terramycin 50</i> [Oxytetracycline]
<i>Geomycin 200</i> [Oxytetracycline]	<i>Terramycin 100</i> [Oxytetracycline]
<i>Kelamycin</i> [Oxytetracycline]	<i>Terramycin 200</i> [Oxytetracycline]
<i>Liquamycin LA-200</i> [Oxytetracycline]	<i>Terramycin-50</i> [Oxytetracycline]

<i>Maxim-200</i> [Oxytetracycline]	<i>Terramycin-100</i> [Oxytetracycline]
<i>Onycin 62.5</i> [Tetracycline]	<i>Terramycin-200</i> [Oxytetracycline]
<i>Onycin 250</i> [Tetracycline]	<i>Terramycin-Aqua</i> [Oxytetracycline]
<i>Onycin 1000</i> [Tetracycline]	<i>Terramycin 100 For Fish</i> [Oxytetracycline]
<i>OT 200</i> [Oxytetracycline]	<i>Terramycin Scours Tablets</i> [Oxytetracycline]
<i>OTC 50</i> [Oxytetracycline]	<i>Terramycin Soluble Powder</i> [Oxytetracycline]
<i>OXTC 50</i> [Oxytetracycline]	<i>Terramycin-343 Soluble Powder</i> [Oxytetracycline]
<i>OXTC 100</i> [Oxytetracycline]	<i>Terra-Vet 100</i> [Oxytetracycline]
<i>OXTC 200</i> [Oxytetracycline]	<i>Terra-Vet Soluble Powder</i> [Oxytetracycline]
<i>Oxy-110</i> [Oxytetracycline]	<i>Terra-Vet Soluble Powder 343</i> [Oxytetracycline]
<i>Oxy-220</i> [Oxytetracycline]	<i>Tet-324</i> [Tetracycline]
<i>Oxy 250</i> [Oxytetracycline]	<i>Tetra 55</i> [Tetracycline]
<i>Oxy-440</i> [Oxytetracycline]	<i>Tetra 250</i> [Tetracycline]
<i>Oxy 1000</i> [Oxytetracycline]	<i>Tetra 1000</i> [Tetracycline]
<i>Oxybiotic-100</i> [Oxytetracycline]	<i>Tetra 4000</i> [Tetracycline]
<i>Oxybiotic-200</i> [Oxytetracycline]	<i>Tetra Bac 324</i> [Tetracycline]
<i>Oxy 500 Calf Bolus</i> [Oxytetracycline]	<i>Tetrabol</i> [Tetracycline]
<i>Oxy 1000 Calf Bolus</i> [Oxytetracycline]	<i>Tetracycline 250</i> [Tetracycline]
<i>Oxycure 100</i> [Oxytetracycline]	<i>Tetracycline 1000</i> [Tetracycline]
<i>Oxycure 200</i> [Oxytetracycline]	<i>Tetracycline 250 Concentrate</i> <i>Soluble Powder</i> [Tetracycline]
<i>Oxy LA</i> [Oxytetracycline]	<i>Tetracycline 62.5 Soluble Powder</i> [Tetracycline]
<i>Oxy LP</i> [Oxytetracycline]	<i>Tetradure LA 300</i> [Oxytetracycline]
<i>Oxy-Mycin 100</i> [Oxytetracycline]	<i>Tetraject LA</i> [Oxytetracycline]
<i>Oxy-Mycin 200</i> [Oxytetracycline]	<i>Tetraject LP</i> [Oxytetracycline]
<i>Oxymycine LA</i> [Oxytetracycline]	<i>Tetramed 250</i> [Tetracycline]
<i>Oxymycine LP</i> [Oxytetracycline]	<i>Tetramed 1000</i> [Tetracycline]
<i>Oxyshot LA</i> [Oxytetracycline]	<i>Tetrasol Soluble Powder</i> [Tetracycline]
<i>Oxysof-62.5</i> [Oxytetracycline]	<i>Tetravet-CA</i> [Oxytetracycline]
<i>Oxysof-110</i> [Oxytetracycline]	<i>Tet-Sol 10</i> [Tetracycline]
<i>Oxysof-220</i> [Oxytetracycline]	<i>Tet-Sol 324</i> [Tetracycline]
<i>Oxysof-250</i> [Oxytetracycline]	<i>Tetroxy-100</i> [Oxytetracycline]
<i>Oxysof-440</i> [Oxytetracycline]	<i>Tetroxy HCA Soluble Powder</i> [Oxytetracycline]
<i>Oxysof-1000</i> [Oxytetracycline]	<i>5-Way Calf Scour Bolus</i> [Tetracycline]
For human-labeled products—	
<i>Achromycin V</i> [Tetracycline]	<i>Novo-Doxylin</i> [Doxycycline]
<i>Alti-Doxycycline</i> [Doxycycline]	<i>Novo-Tetra</i> [Tetracycline]
<i>Apo-Doxy</i> [Doxycycline]	<i>Nu-Doxycycline</i> [Doxycycline]
<i>Apo-Doxy-Tabs</i> [Doxycycline]	<i>Nu-Tetra</i> [Tetracycline]
<i>Apo-Tetra</i> [Tetracycline]	<i>Vibramycin</i> [Doxycycline]
<i>Doryx</i> [Doxycycline]	<i>Vibra-Tabs</i> [Doxycycline]
<i>Doxylin</i> [Doxycycline]	<i>Vibra-Tabs C-Pak</i> [Doxycycline]
<i>Doxytec</i> [Doxycycline]	

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

**Category:** Antibacterial (systemic); antiprotozoal; antirickettsial.

## Indications

Note: Bracketed information in the *Indications* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

## General considerations

The tetracyclines are broad-spectrum antibiotics with activity against gram-positive and gram-negative bacteria, including some anaerobes. They are also active against chlamydia, mycoplasmas, some protozoa {R-28; 133}, and several rickettsiae, including *Anaplasma*, *Ehrlichia*, and *Haemobartonella*. The activity range of the tetracyclines also includes *Escherichia coli*, *Klebsiella* species, *Pasteurella* species, *Salmonella* species, *Staphylococcus* species, and *Streptococcus* species {R-4}. Susceptibility testing has demonstrated that some coliforms, mycoplasma, streptococci, and staphylococci have developed resistance to tetracyclines {R-21; 150}. However, the breakpoints used to classify these organisms as susceptible or resistant are not validated for animal indications. Susceptibility testing should not be the sole basis for selecting tetracyclines for therapy {R-65}.

#### Accepted

**Abortion, vibronic (prophylaxis)<sup>1</sup>—Sheep:** Chlortetracycline for medicated feed {R-16; 152} is indicated to aid in reduction of the incidence of vibronic abortion caused by susceptible *Campylobacter fetus*.

**Abscesses, cervical (prophylaxis)<sup>1</sup>—Pigs:** Chlortetracycline for medicated feed {R-152} is indicated for reduction of the incidence of cervical abscesses caused by susceptible organisms.

**Abscesses, hepatic (prophylaxis)<sup>1</sup>—Cattle:** Chlortetracycline for medicated feed {R-16; 152} is indicated as an aid in the prevention of hepatic abscesses in cattle.

**Actinobacillosis (treatment)<sup>1</sup>—Cattle:** Oxytetracycline injection {R-10; 45} is indicated in the treatment of actinobacillosis (wooden tongue) caused by susceptible *Actinobacillus lignieresii*.

**Anaplasmosis (treatment)<sup>1</sup>—Cattle:** Chlortetracycline for medicated feed {R-16; 152} is indicated in the control of active infection caused by susceptible *Anaplasma marginale*. Oxytetracycline injection {R-10} is indicated in the treatment of anaplasmosis caused by susceptible *A. marginale*.

**Diphtheria (treatment)<sup>1</sup>—Cattle:** Oxytetracycline injection {R-10; 24; 45} is indicated in the treatment of diphtheria (necrotic laryngitis, necrotic necrophorus stomatitis) caused by susceptible *Fusobacterium necrophorum*.

**Enteritis, bacterial (treatment)**—The treatment of enteritis should be dependent on a specific diagnosis and knowledge of pathogen susceptibility to tetracyclines. Some pathogens associated with enteritis, such as *Escherichia coli*, are found to be resistant to the tetracyclines.

**Calves:** Chlortetracycline soluble powder<sup>1</sup> {R-17}, oxytetracycline tablets {R-60}, and tetracycline boluses and soluble powder {R-1; 8} are indicated in the control of bacterial enteritis (scours) caused by susceptible *E. coli*. Chlortetracycline for medicated feed {R-16; 152} and soluble powder {R-17}; oxytetracycline for medicated feed {R-117}, injection, soluble powder, and tablets<sup>1</sup> {R-23; 24; 60; 61}; and tetracycline bolus and soluble powder {R-1; 18} are indicated in the treatment of bacterial enteritis caused by susceptible *E. coli* and *Salmonella* species.

**Cattle:** Chlortetracycline for medicated feed<sup>1</sup> {R-16; 152} and oxytetracycline for medicated feed<sup>1</sup> {R-117}, injection<sup>1</sup> {R-10; 45}, and soluble powder {R-61} are indicated in the treatment of bacterial enteritis caused by susceptible *E. coli* and *Salmonella* {R-11}.

**Pigs:** Chlortetracycline soluble powder<sup>1</sup> {R-17}, oxytetracycline soluble powder {R-11; 23; 54}, and tetracycline powder for oral solution {R-18} are indicated in the control and treatment of bacterial enteritis caused by susceptible *E. coli*. Chlortetracycline for medicated feed {R-16; 152} and oxytetracycline injection {R-24; 45} and for medicated feed {R-117} are indicated in the treatment of bacterial enteritis (scours) caused by susceptible *E. coli* and *Salmonella*.

**Sheep:** Oxytetracycline for medicated feed<sup>1</sup> {R-117} and soluble powder {R-54; 61} and [tetracycline soluble powder] {R-18} are indicated in the treatment of enteritis caused by susceptible organisms.

**Sows:** Oxytetracycline injection {R-10} is indicated in the control of enteritis (baby pig scours) in suckling pigs caused by susceptible

*E. coli* and is administered by treatment of sows before and after farrowing; however, the effect of this treatment on piglets may be indirect, through the resolution of mastitis and increase in milk production in sows **{R-171}**.

*Turkeys, growing:* Chlortetracycline soluble powder<sup>1</sup> **{R-17}** and oxytetracycline soluble powder **{R-11; 23; 54}** are indicated in the control of susceptible organisms involved in the development of enteritis (bluecomb).

*Turkeys:* Chlortetracycline for medicated feed **{R-16; 152}** and [powder for oral solution] **{R-17}** and tetracycline soluble powder **{R-18; 19}** are indicated in the control and treatment of enteritis caused by susceptible organisms. Oxytetracycline for medicated feed **{R-117}** is indicated in the treatment of susceptible *E. coli* involved in the development of enteritis (bluecomb).

[*Chickens*]: Oxytetracycline soluble powder **{R-54}** and chlortetracycline for medicated feed are indicated in the treatment of susceptible *E. coli* involved in the development of enteritis.

[*Lambs*]: Oxytetracycline for medicated feed **{R-26}** is indicated in the reduction of bacterial enteritis in creep-fed suckling lambs.

*Escherichia coli* infections (treatment)<sup>1</sup>—*Chickens:* Chlortetracycline for medicated feed **{R-16; 115; 152}** is indicated as an aid in reducing mortality due to *E. coli* infections.

Feed efficiency, improved; or

Weight gain, increased rate—*Calves*<sup>1</sup>, *cattle*<sup>1</sup>, *chickens, pigs, sheep*<sup>1</sup>, and *turkeys:* Chlortetracycline for medicated feed **{R-16; 152}** and oxytetracycline for medicated feed<sup>1</sup> **{R-117}** are indicated for growth promotion and feed efficiency.

Foul brood (treatment)—*Bees:* Oxytetracycline for medicated feed **{R-117}** and soluble powder **{R-61; 117}** are indicated in the treatment of American and European foul brood caused by susceptible organisms.

Fowl cholera (prophylaxis)—*Chickens:* Oxytetracycline for medicated feed **{R-122}** and soluble powder<sup>1</sup> **{R-61; 122}** are indicated in the prevention of fowl cholera caused by susceptible organisms.

Fowl cholera (treatment)—

*Chickens:* Chlortetracycline soluble powder<sup>1</sup> **{R-17}** and oxytetracycline for medicated feed<sup>1</sup> **{R-117}** and soluble powder **{R-11}** are indicated in the control of mortality from fowl cholera caused by susceptible *Pasteurella multocida* **{R-80}**. [Tetracycline soluble powder **{R-18}** is indicated in the treatment of fowl cholera caused by susceptible organisms.]

*Ducks*<sup>1</sup>: Chlortetracycline for medicated feed **{R-152}** is indicated as an aid in the control and treatment of fowl cholera caused by susceptible *Pasteurella multocida*.

Furunculosis (treatment)—*Salmonids* (salmon and trout): Oxytetracycline for medicated feed **{R-62; 124}** is indicated in the control of furunculosis caused by susceptible *Aeromonas salmonicida*.

Gaffkemia (treatment)—*Lobsters:* Oxytetracycline for medicated feed **{R-27; 124}** is indicated in the treatment of gaffkemia caused by susceptible *Aerococcus viridans*.

Gastroenteritis (treatment)—*Cats and dogs:* Tetracycline oral suspension **{R-4}** is indicated in the treatment of bacterial gastroenteritis, but use should be reserved for treatment of organisms known to be susceptible.

Hemorrhagic septicemia, bacterial (treatment)<sup>1</sup>—*Catfish and salmonids:* Oxytetracycline for medicated feed **{R-62; 124}** is indicated in the control of hemorrhagic septicemia caused by susceptible *Aeromonas hydrophila*, *A. sobia*, and *Pseudomonas* species **{R-173}**.

Hexamitiasis (treatment)—*Turkeys:* Chlortetracycline for medicated feed<sup>1</sup> **{R-16; 152}** and oxytetracycline for medicated feed<sup>1</sup> **{R-117}** are indicated in the control of hexamitiasis, and oxytetracycline soluble powder<sup>1</sup> **{R-11; 61}** and [tetracycline soluble powder] **{R-18}** are indicated in the treatment of hexamitiasis caused by susceptible *Hexamita meleagridis*.

Keratoconjunctivitis, infectious (treatment)—*Cattle:* Long-acting oxytetracycline injection **{R-45}** is indicated in the treatment of keratoconjunctivitis caused by susceptible *Moraxella bovis*.

Leptospirosis (treatment)—

*Pigs:* Chlortetracycline for medicated feed<sup>1</sup> **{R-16; 152}** and oxytetracycline for medicated feed **{R-122}** are indicated to aid in reducing the shedding of leptospirosis and the incidence of

abortion. Oxytetracycline for medicated feed is indicated as an aid in the reduction of abortion and urinary shedding of leptospirosis, production of healthier newborn pigs, and maintenance of weight gains in the presence of leptospirosis {**R-122**}. Oxytetracycline injection {**R-10; 24; 45**} and soluble powder {**R-11**} are indicated in the treatment of leptospirosis caused by susceptible *Leptospira pomona*. Oxytetracycline can reduce the incidence of abortions and shedding of leptospira; {**R-11**} however, it can be ineffective in eliminating the organism {**R-113**}.

*Cattle*: Oxytetracycline injection {**R-24; 45**} is indicated in the treatment of leptospirosis caused by susceptible *Leptospira pomona*.

Paratyphoid (treatment)<sup>1</sup>—*Turkeys*, less than 4 weeks of age:

Chlortetracycline for medicated feed {**R-16; 152**} is indicated as an aid in reducing mortality from paratyphoid infection caused by susceptible *Salmonella typhimurium*.

Pneumonia, bacterial (prophylaxis)—*Cattle*: Oxytetracycline for medicated feed {**R-117; 122**} is indicated in the prevention of pneumonia and as an aid in the reduction of losses due to bovine respiratory disease complex.

Pneumonia, bacterial (treatment)—

*Calves*: Chlortetracycline soluble powder<sup>1</sup> {**R-17**}, oxytetracycline tablets<sup>1</sup> {**R-60**}, and tetracycline boluses {**R-1**} are indicated in the control of pneumonia and bovine respiratory disease complex caused by susceptible organisms, including *Pasteurella* species. Chlortetracycline soluble powder {**R-17**}; oxytetracycline injection, soluble powder, and tablets<sup>1</sup> {**R-60; 61**}; and tetracycline boluses and soluble powder {**R-1; 18**} are indicated in the treatment of pneumonia caused by susceptible organisms, including *Pasteurella* species. However, due to resistance {**R-51; 171; 180**} by pathogens, the tetracyclines may no longer be effective in the treatment of some types of bacterial pneumonia.

*Cattle*: Chlortetracycline for medicated feed {**R-152**} is indicated in the control<sup>1</sup> and treatment of pneumonia caused by susceptible organisms. Oxytetracycline {**R-10; 24; 45; 61**} is indicated in the treatment of pneumonia and shipping fever complex caused by susceptible *Pasteurella* and *Haemophilus* species. Increasing resistance to tetracyclines by strains of organisms involved in bovine pneumonia is reported {**R-51; 171; 180**}.

*Pigs*: Chlortetracycline soluble powder<sup>1</sup> {**R-17**} is indicated in the control of pneumonia caused by susceptible *Actinobacillus pleuropneumoniae* (*Haemophilus* species), *Pasteurella* species, and *Klebsiella* species. Chlortetracycline for medicated feed {**R-152**} and oxytetracycline soluble powder are indicated in the treatment of pneumonia caused by susceptible *Pasteurella multocida*. Chlortetracycline soluble powder {**R-17**}, oxytetracycline injection {**R-10; 24; 45**}, and tetracycline soluble powder {**R-1; 18**} are indicated in the treatment of pneumonia caused by susceptible *Actinobacillus pleuropneumonia* (*Haemophilus* species), *Klebsiella*, and *Pasteurella* species. Increasing resistance to tetracycline by strains of organisms involved in porcine pneumonia is reported {**R-50**}.

*Sheep*: Oxytetracycline for medicated feed<sup>1</sup> {**R-117**}, [injection] {**R-24; 121**}, and soluble powder {**R-6; 13**}, and [tetracycline soluble powder] {**R-18**} are indicated in the treatment of pneumonia caused by susceptible organisms.

Pododermatitis (treatment)—*Cattle*: Long-acting oxytetracycline injection {**R-10; 24; 45**} is indicated in the treatment of pododermatitis ('foot rot') caused by susceptible *Fusobacterium necrophorum*. Signs may not be completely resolved by oxytetracycline alone and other treatment or surgery may be required.

Pseudomonas disease (treatment)<sup>1</sup>—*Catfish* and *salmonids*:

Oxytetracycline for medicated feed {**R-62**} is indicated in the control of pseudomonas disease caused by susceptible organisms.

Psittacosis (treatment)<sup>1</sup>—*Cockatoos*, *macaws*, and *parrots*:

Chlortetracycline for medicated feed {**R-152**} is indicated in the treatment of psittacosis caused by susceptible *Chlamydia psittaci*.

Respiratory disease, bacterial, chronic (prophylaxis)—*Chickens*:

Oxytetracycline for medicated feed {**R-122**} is indicated in the

- prevention of chronic respiratory disease caused by susceptible organisms.
- Respiratory disease, bacterial, chronic (treatment)—*Chickens*: Chlortetracycline for medicated feed and soluble powder {**R-16; 17; 152**}, oxytetracycline for medicated feed<sup>1</sup> and soluble powder {**R-11; 22; 23**}, and tetracycline soluble powder {**R-18; 127**} are indicated in the control of respiratory disease, including air sac disease, caused by susceptible *Mycoplasma gallisepticum* and *E. coli*. Chlortetracycline for medicated feed {**R-16; 115**} and powder for oral solution {**R-17**} are indicated in the treatment of chronic respiratory disease caused by susceptible organisms.
- Skeletal tissue marking<sup>1</sup>—*Salmon, Pacific*: Oxytetracycline for medicated feed {**R-117**} is indicated to mark skeletal tissue in Pacific salmon.
- Skin and soft tissue infections (treatment)<sup>1</sup>—*Cattle*: {**R-10; 45**} Oxytetracycline injection is indicated in the treatment of wounds infected by susceptible *Staphylococcus* species or *Streptococcus* species.
- Synovitis, infectious (treatment)—*Chickens and turkeys*: Chlortetracycline for medicated feed<sup>1</sup> {**R-16; 152**} and soluble powder<sup>1</sup> {**R-17**}, oxytetracycline for medicated feed {**R-117**} and soluble powder {**R-11**}, and tetracycline soluble powder {**R-3**} are indicated in the control of infectious synovitis caused by susceptible *Mycoplasma synoviae*. Chlortetracycline powder for oral solution {**R-17**} is indicated in the treatment of infectious synovitis caused by susceptible *M. synoviae*.
- Ulcer disease (treatment)—*Salmonids* (salmon, trout): Oxytetracycline for medicated feed {**R-62; 124**} is indicated in the control of ulcer disease caused by susceptible *Haemophilus piscium*.
- Urinary tract infections (treatment)—*Cats and dogs*: Tetracycline oral suspension {**R-4**} is indicated in the treatment of urinary tract infections caused by susceptible *Staphylococcus* species and *E. coli*. Also, concentrations of tetracycline in urine are high enough to be effective against *Pseudomonas* species {**R-150**}.
- Uterine infections, acute (treatment)—*Cattle*: Oxytetracycline injection {**R-24; 45**} is indicated in the treatment of acute metritis caused by susceptible strains of *Staphylococcus* and *Streptococcus* species.  
 [*Pigs*]: Oxytetracycline injection {**R-24**} is indicated in the treatment of acute metritis caused by susceptible organisms.  
 [*Sheep*]: Oxytetracycline injection {**R-24; 121**} is indicated in the treatment of uterine infections.
- [Arthritis, bacterial (treatment)]—*Cattle and sheep*: Oxytetracycline injection {**R-24; 25**} is indicated in the treatment of septic arthritis (joint ill) caused by susceptible organisms.
- [Atrophic rhinitis (treatment)]—*Pigs*: Oxytetracycline for medicated feed {**R-122**} is indicated for use as an aid in maintaining weight gain in pigs infected with atrophic rhinitis.
- [Blackleg (treatment)]; or
- [Malignant edema (treatment)]—*Cattle*: Oxytetracycline injection {**R-24; 25; 121**} is indicated in the treatment of infections caused by susceptible *Clostridia* species.
- [Bloat]—*Cattle*: Oxytetracycline for medicated feed {**R-26**} is indicated as an aid in reducing the incidence of bloat in young cattle on pasture and in feedlots.
- [Cold water disease (treatment)]—*Salmonids*: {**R-124**} Oxytetracycline for medicated feed is indicated in the treatment of cold water disease caused by susceptible *Cytophaga psychrophilia*.
- [Columnaris disease (treatment)]—*Salmonids*: Oxytetracycline for medicated feed {**R-124**} is indicated in the treatment of columnaris disease caused by susceptible *Chondrococcus (Flexibacter) columnaris*.
- [Egg production, increased]; or
- [Egg hatchability, increased]—*Chickens and turkeys*: Chlortetracycline for medicated feed is indicated for use in increasing egg production or egg hatchability.
- [Ehrlichiosis, equine (treatment)]<sup>1</sup>—*Horses*: Oxytetracycline is used in the treatment of ehrlichiosis caused by susceptible *Ehrlichia equi* {**R-46; 138**}.
- [Enteric redmouth disease (treatment)]—*Salmonids*: Oxytetracycline for medicated feed {**R-124**} is indicated in the treatment of enteric red-

- mouth disease caused by susceptible *Yersinia ruckeri*.
- [Enterotoxemia (treatment)]—*Lambs*: Chlortetracycline for medicated feed and oxytetracycline for medicated feed {**R-26**} are indicated in the reduction of losses due to enterotoxemia in feedlot lambs.
- [Erysipelas (treatment)]—*Pigs*: Oxytetracycline injection {**R-24; 25; 121**} is indicated in the treatment of erysipelas caused by susceptible organisms.
- [Mastitis (treatment)]—*Cattle, pigs, and sheep*: Oxytetracycline injection {**R-24; 25**} is indicated in the treatment of mastitis caused by susceptible organisms. Oxytetracycline, administered at the dosage recommended in product labeling, does not appear to be effective for the cure of *Staphylococcus aureus* infections in the dry cow {**R-103**}.
- [Omphalophlebitis (treatment)]—*Cattle*: Oxytetracycline injection {**R-24; 25**} is indicated in the treatment of omphalophlebitis (navel ill) caused by susceptible organisms.
- [Peritonitis (treatment)]—*Cattle*: Oxytetracycline injection {**R-25; 121**} is indicated in the treatment of peritonitis caused by susceptible organisms.
- [Pododermatitis (prophylaxis)]—*Cattle*: Chlortetracycline for medicated feed is indicated as an aid in the prevention of pododermatitis {**R-116**}.
- [Potomac horse fever (treatment)]<sup>1</sup>—*Horses*: Oxytetracycline is used in the treatment of Potomac horse fever (equine ehrlichial colitis) caused by susceptible *Ehrlichia risticii* {**R-47; 48**}. Treatment of exposed animals to prevent development of disease is not recommended; the incubation period will be increased but the disease is not prevented {**R-48**}.
- [Rocky Mountain spotted fever (treatment)]<sup>1</sup>—*Dogs*: Tetracycline or doxycycline {**R-151**} is used in the treatment of Rocky Mountain spotted fever caused by susceptible *Rickettsia rickettsii* {**R-140; 141**}.
- [Sinusitis, infectious (prophylaxis)]—*Turkeys*: Chlortetracycline for medicated feed is indicated in the prevention of sinusitis caused by susceptible organisms.
- [Sinusitis, infectious (treatment)]—*Turkeys*: Oxytetracycline for medicated feed {**R-26; 122**} and tetracycline soluble powder are indicated in the control of sinusitis caused by susceptible organisms, such as susceptible *Mycoplasma gallisepticum*.

#### Acceptance not established

- [Brucellosis (treatment)]<sup>1</sup>—*Dogs*: There are insufficient data to establish the efficacy of tetracycline administered concurrently with streptomycin in the treatment of brucellosis in dogs; however, studies suggest that specific dosage regimens may be successful in treating the infection {**R-160**}. No controlled studies are available.
- [Chlamydial infection (treatment)]<sup>1</sup>; or
- [Respiratory tract infections, bacterial (treatment)]<sup>1</sup>—*Cats*: There are insufficient data to establish the safety and efficacy of doxycycline in the treatment of chlamydial infections or bacterial respiratory infections in cats; however, it is used in the treatment of infections caused by susceptible organisms {**R-151; 177**}.
- [Ehrlichiosis (treatment)]<sup>1</sup>—*Dogs*: There are insufficient data to establish the efficacy of doxycycline in the treatment of ehrlichiosis in dogs. Clinical signs are often resolved by administration of doxycycline or tetracycline {**R-40; 41; 43; 139**}, but it is uncertain whether the organism is cleared from dogs treated {**R-40; 139**}. Serum *Ehrlichia canis* antibody titers can remain increased in some dogs for over 2 years after the resolution of clinical signs during treatment with tetracycline {**R-139**}; also, in some dogs, blood and tissue cultures have tested positive for *Ehrlichia canis* 2 months after treatment with doxycycline {**R-40**}.
- [Flexural limb deformities (treatment)]<sup>1</sup>—*Foals*: There are insufficient data to establish the efficacy of oxytetracycline in the treatment of flexural limb deformities in foals; however, studies show that oxytetracycline can cause a short-term moderate improvement in metacarpophalangeal joint angle and an increase in range of joint motion in newborn foals as compared to untreated foals {**R-157; 158**}. The available studies were performed in healthy foals rather than foals with deformities and both the ideal dose and actual short- and long-term benefits and risks of this treatment are unknown.
- [*Haemobartonella felis* infection (treatment)]<sup>1</sup>—*Cats*: There are

insufficient data to establish the safety and efficacy of doxycycline in the treatment of feline infectious anemia, caused by susceptible *Haemobartonella felis*; however, it is used in the treatment of acute infections {**R-147**}. If considered clinically necessary, corticosteroids {**R-149**} and blood transfusions are used concurrently with doxycycline in the treatment of this infection {**R-147**}. Acutely infected cats may clinically recover without treatment {**R-147**; **159**}, although it is believed that the organism is not cleared from these animals; there is also some question about the efficacy of doxycycline or other tetracyclines in completely clearing the organism from infected cats {**R-148**}. Controlled clinical efficacy trials have not been conducted for any medication; however, a tetracycline is usually administered when a cat is diagnosed and doxycycline is considered the tetracycline of choice {**R-147**} because of an expectation of fewer side effects. Cats with serious underlying viral infections, such as feline leukemia virus, are not expected to respond well to therapy.

[Leptospirosis (treatment)]<sup>1</sup>—*Dogs*: Although doxycycline is proposed in some veterinary references for use in the clearance of the leptospirosis carrier state in dogs, there are insufficient data showing clearance or prevention of a potential carrier state to support this use as an established indication.

[Lyme disease (treatment)]<sup>1</sup>—*Dogs*: There are insufficient data to establish the efficacy of tetracyclines in the treatment of Lyme borreliosis. Doxycycline has been effective in the resolution of early *Borrelia burgdorferi* infection in people {**R-163**}; therefore, doxycycline and tetracycline are used to treat the infection in dogs {**R-164**; **165**}; however, it is uncertain whether this is the best medication to produce long-term resolution of the infection {**R-163**}.

[Thromboembolic meningoencephalitis (treatment)]<sup>1</sup>—*Cattle*: There are insufficient data to establish the efficacy of oxytetracycline in the treatment of thromboembolic meningoencephalitis; however, if cattle are diagnosed in the early stages of the disease, before recumbency, treatment can be effective against susceptible *Haemophilus somnus* {**R-161**; **166**}.

[Uterine infections, bacterial (treatment)]—*Cattle, horses, pigs, and sheep*: Although Canadian product labeling includes the use of *intrauterine* chlortetracycline, oxytetracycline, and tetracycline in the treatment of uterine infections, there are insufficient available data concerning the efficacy and safety of this use. Intrauterine tetracycline treatment can reduce the incidence of putrefaction of retained fetal membranes and fever associated with infection in cattle, but because it is believed to penetrate only into the endometrium from infusion into the uterus {**R-104**; **130**}, parenteral antibiotics are recommended for those animals that have evidence of infection or develop signs of septicemia {**R-144**}. The intrauterine administration of tetracyclines for the treatment of uterine infections such as endometritis or treatment of infection associated with retained placentas in cattle is not effective in shortening the interval from parturition to conception, increasing pregnancy rates, or reducing culling rates {**R-144-146**}. Considering costs, risks of residues {**R-129**}, and a lack of significant change in long-term fertility in cattle, there is no evidence to support the routine use of intrauterine tetracyclines in cattle, horses, pigs, and sheep.

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## Regulatory Considerations

### U.S.—

Withdrawal times have been established for chlortetracycline for medicated feed and soluble powder; oxytetracycline soluble powder, for medicated feed, tablets, and injection; and tetracycline soluble powder and boluses. See the *Dosage Forms* section.

### Canada—

Withdrawal times have been established for chlortetracycline for medicated feed and uterine tablets; oxytetracycline soluble powder, for medicated feed, uterine infusion, and injection; and tetracycline soluble powder, boluses, and uterine tablets. See the

Dosage Forms section.

## Chemistry

### Source:

- Chlortetracycline—Isolated from the fungus *Streptomyces aureofaciens* {R-22}.  
Doxycycline—Produced semisynthetically. {R-22}  
Oxytetracycline—Isolated from the fungus *Streptomyces rimosus* {R-22}.  
Tetracycline—Produced by some streptomyces strains; however, it is manufactured by hydrogenolysis of chlortetracycline {R-113}.

### Chemical name:

- Chlortetracycline hydrochloride—2-Naphthacenecarboxamide, 7-chloro-4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, monohydrochloride [4S-(4 alpha,4a alpha,5a alpha,6 beta,12a alpha)]- {R-114}.  
Doxycycline—2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, [4S-(4 alpha,4a alpha,5 alpha,5a alpha,6 alpha,12a alpha)]-, monohydrate {R-114}.  
Doxycycline hyclate—2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, monohydrochloride, compd. with ethanol (2:1), monohydrate, [4S-(4 alpha, 4a alpha, 5 alpha, 5a alpha, 6 alpha, 12a alpha)]- {R-114}.  
Oxytetracycline—2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-, [4S-(4 alpha,4a alpha,5 alpha,5a alpha,6 beta,12a alpha)]-, dihydrate {R-114}.  
Oxytetracycline hydrochloride—2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxo-, monohydrochloride, [4S-(4 alpha,4a alpha,5 alpha,5a alpha,6 beta,12a alpha)]- {R-114}.  
Tetracycline—2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, [4S-(4 alpha,4a alpha,5a alpha,6 beta,12a alpha)]- {R-114}.  
Tetracycline hydrochloride—2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, monohydrochloride, [4S-(4 alpha,4a alpha,5a alpha,6 beta,12a alpha)]- {R-114}.

### Molecular formula:

- Chlortetracycline hydrochloride— $C_{22}H_{23}ClN_2O_8 \cdot HCl$  {R-114}.  
Doxycycline— $C_{22}H_{24}N_2O_8 \cdot H_2O$  {R-114}.  
Doxycycline hyclate— $(C_{22}H_{24}N_2O_8 \cdot HCl)_2 \cdot C_2H_6O \cdot H_2O$  {R-114}.  
Oxytetracycline— $C_{22}H_{24}N_2O_9 \cdot 2H_2O$  {R-114}.  
Oxytetracycline hydrochloride— $C_{22}H_{24}N_2O_9 \cdot HCl$  {R-114}.  
Tetracycline— $C_{22}H_{24}N_2O_8$  {R-114}.  
Tetracycline hydrochloride— $C_{22}H_{24}N_2O_8 \cdot HCl$  {R-114}.

### Molecular weight:

- Chlortetracycline hydrochloride—515.34 {R-114}.  
Doxycycline—462.45 {R-114}.  
Doxycycline hyclate—1025.87 {R-114}.  
Oxytetracycline—496.46 {R-114}.  
Oxytetracycline hydrochloride—496.89 {R-114}.  
Tetracycline—444.43 {R-114}.  
Tetracycline hydrochloride—480.90 {R-114}.

### Description:

- Chlortetracycline Hydrochloride USP—Yellow, crystalline powder. Is odorless. Is stable in air, but is slowly affected by light {R-128}.  
Doxycycline USP—Yellow, crystalline powder {R-128}.  
Doxycycline Hyclate USP—Yellow, crystalline powder {R-128}.  
Oxytetracycline USP—Pale yellow to tan, odorless, crystalline powder. Is stable in air, but exposure to strong sunlight causes it to darken. It loses potency in solutions of pH below 2, and is rapidly destroyed by alkali hydroxide solutions {R-128}.  
Oxytetracycline Hydrochloride USP—Yellow, odorless, crystalline powder. Is hygroscopic. Decomposes at a temperature exceeding

180 °C, and exposure to strong sunlight or to temperatures exceeding 90 °C in moist air causes it to darken. Its potency is diminished in solutions having a pH below 2, and is rapidly destroyed by alkali hydroxide solutions **{R-128}**.

Tetracycline USP—Yellow, odorless, crystalline powder. Is stable in air, but exposure to strong sunlight causes it to darken. It loses potency in solutions of pH below 2, and is rapidly destroyed by alkali hydroxide solutions **{R-128}**.

Tetracycline Hydrochloride USP —Yellow, odorless, crystalline powder. Is moderately hygroscopic. Is stable in air, but exposure to strong sunlight in moist air causes it to darken. It loses potency in solution at a pH below 2, and is rapidly destroyed by alkali hydroxide solutions **{R-128}**.

**pKa:**

Chlortetracycline: 3.3, 7.4, 9.3 **{R-133}**.

Oxytetracycline: 3.3, 3.7, 9.1 **{R-156}**.

Tetracycline: 8.3, 10.2 **{R-133}**.

**Solubility:**

Chlortetracycline Hydrochloride USP—Sparingly soluble in water; soluble in solutions of alkali hydroxides and carbonates; slightly soluble in alcohol; practically insoluble in acetone, in chloroform, in dioxane, and in ether **{R-128}**.

Doxycycline USP—Very slightly soluble in water; freely soluble in dilute acid and in alkali hydroxide solutions; sparingly soluble in alcohol; practically insoluble in chloroform and in ether **{R-128}**.

Doxycycline Hyclate USP—Soluble in water and in solutions of alkali hydroxides and carbonates; slightly soluble in alcohol; practically insoluble in chloroform and in ether **{R-128}**.

Oxytetracycline USP —Very slightly soluble in water; freely soluble in 3 *N* hydrochloric acid and in alkaline solutions; sparingly soluble in alcohol **{R-128}**.

Oxytetracycline Hydrochloride USP —Freely soluble in water, but crystals of oxytetracycline base separate as a result of partial hydrolysis of the hydrochloride. Sparingly soluble in alcohol and in methanol, and even less soluble in dehydrated alcohol; insoluble in chloroform and in ether **{R-128}**.

Tetracycline USP—Very slightly soluble in water; freely soluble in dilute acid and in alkali hydroxide solutions; sparingly soluble in alcohol; practically insoluble in chloroform and in ether **{R-128}**.

Tetracycline Hydrochloride USP —Soluble in water and in solutions of alkali hydroxides and carbonates; slightly soluble in alcohol; practically insoluble in chloroform and in ether **{R-128}**.

## Pharmacology/Pharmacokinetics

Note: Unless otherwise noted, pharmacokinetic values are based on a single intravenous dose of medication.

**Mechanism of action/Effect:**

Tetracyclines are broad-spectrum bacteriostatic agents that inhibit protein synthesis by binding reversibly to receptors of the 30 S ribosomal subunit of susceptible microorganisms. The binding of a tetracycline to the subunit blocks the binding of the aminoacyl-tRNA to the acceptor site on the mRNA-ribosomal complex and prevents the addition of new amino acids to the peptide chain, inhibiting protein synthesis. **{R-22}**

Tetracyclines must enter the target cell to be effective. Uptake appears to depend on passive diffusion and active transport, with the exception of doxycycline, which enters the cell by passive diffusion **{R-28}**. Susceptible cells concentrate the antibiotic; resistant strains appear to carry an R-factor that inhibits uptake of drug. **{R-22}**

**Absorption:**

Oral—Doxycycline: Generally is more completely absorbed from the gastrointestinal tract than are the tetracyclines developed less recently **{R-40; 64; 74}**, which can be poorly and variably absorbed. Human studies have shown that the absorption of oxytetracycline or tetracycline is decreased when either is administered with food; the effect of food on doxycycline absorption is insignificant. Doxycycline is also less likely than the

older tetracyclines to form chelation complexes with divalent and trivalent metals and, therefore, there is less interference with oral absorption by calcium or other substances **{R-133}**. See the *Drug interactions* section.

Parenteral—Oxytetracycline: As with other parenteral medications, the absorption and bioavailability of intramuscularly administered oxytetracycline can vary depending on the site of administration. Oxytetracycline is more bioavailable when administered intramuscularly into the shoulder of calves than when administered intramuscularly into the neck or particularly into the buttock. **{R-94}**

The absorption of the long-acting formulations of oxytetracycline (with 2-pyrrolidone excipient) administered intramuscularly has been described as having a rapid phase of 48 minutes for 14% of the dose and a slow phase of 18 hours for 38% of the dose in cattle administered a 20 mg/kg dose **{R-99}**. With a 10 mg/kg dose, the rapid phase is 16 minutes and the slow phase is 11 hours. **{R-100}**

#### Bioavailability:

Oral—

Chlortetracycline:

*Chickens*—1% (25 mg per kg of body weight [mg/kg] dose).

**{R-78; 79}**

*Pigs*—Fasted or fed: 18 to 19% **{R-77}**.

*Turkeys*—6% (15 mg/kg dose). **{R-78; 80}**

Doxycycline:

*Chickens*—41.3% (20 mg/kg dose). **{R-64}**

*Human value*—90 to 95% **{R-169}**.

Oxytetracycline:

*Pigs*—4.8% (50 mg/kg dose). **{R-109}**

*Piglets*, weaned, 10 weeks of age—

By drench: 9% (20 mg/kg dose). **{R-82}**

In medicated feed for 3 days: 3.7% (400 parts per million [ppm] of feed). **{R-82}**

*Trout, rainbow (Oncorhynchus mykiss)*—5.6% (75 mg/kg dose). **{R-89}**

*Turkeys*—

Fasted: 47.6% (10 mg/kg dose). **{R-85}**

Fed: 9.4% (10 mg/kg dose). **{R-85}**

Tetracycline: *Pigs*, fasted—23% (22 mg/kg dose). **{R-74}**

Intramuscular—

Oxytetracycline, conventional formulation:

*Buffalo*—63.2% (22 mg/kg dose). **{R-87}**

*Calves*, 17 days of age—61% (20 mg/kg dose) **{R-99}**.

*Calves*, 3 months of age—76 hours postinjection of 18 mg/kg dose:

Buttock administration—83.1%. **{R-94}**

Neck administration—93.3%. **{R-94}**

Shoulder administration—99.4%. **{R-94}**

*Catfish, African, and trout, rainbow*—85% (60 mg/kg dose). **{R-90}**

*Cows*—80.8% (8 mg/kg dose) **{R-95}**; 95% (20 mg/kg dose) **{R-174}**.

*Goats*—65.5% (20 mg/kg dose). **{R-81}**

Oxytetracycline, long-acting formulation:

*Camels*—93.7% (10 mg/kg dose). **{R-88}**

*Cattle*—51%; 78.5%; 95% (20 mg/kg dose). **{R-98; 99; 174}**

*Goats*—79.4% (20 mg/kg dose). **{R-81}**

**Distribution:** Tetracyclines are lipid soluble and are well distributed to most tissues. Doxycycline is the most lipid soluble and shows the greatest degree of tissue penetration. **{R-28; 71}**

Volume of distribution—

Chlortetracycline:

*Calves*, ruminating—Area volume of distribution:  $1.93 \pm 0.15$  liters per kg (L/kg). **{R-76}**

*Pigs*—Steady state volume of distribution:

Fasted— $0.97 \pm 0.21$  L/kg. **{R-77}**

Fed— $1.39 \pm 0.31$  L/kg. **{R-77}**

*Turkeys*—Area:  $0.23 \pm 0.05$  L/kg. {**R-78**}

Doxycycline:

*Calves*—Steady state:

Preruminating— $1.81 \pm 0.24$  L/kg. {**R-68**}

Ruminating— $1.31 \pm 0.11$  L/kg. {**R-68**}

*Cats*—Steady state:  $0.34 \pm 0.03$  L/kg. {**R-70**}

*Dogs*—Steady state:  $0.93 \pm 0.14$  L/kg. {**R-70**}

*Pigs*—Steady state:  $0.53 \pm 0.04$  L/kg. {**R-69**}

Oxytetracycline:

*Buffalo*—Area: 0.28 to 0.45 L/kg. {**R-87**}

*Calves*, newborn to 8 months—Area: 1.67 L/kg. {**R-93; 100**}

*Camels*—Steady state: 0.71 L/kg. {**R-88**}

*Cows*—Area:  $0.80 \pm 0.03$  L/kg. {**R-95**}

*Dogs*—Area:  $2.10 \pm 0.42$  L/kg. {**R-84**}

*Donkeys*—

Area: 0.78 L/kg {**R-92**},

Steady state: 0.65 L/kg {**R-92**},

*Foals*—

Area: 2.19 L/kg. {**R-154**}

Steady state: 2.17 L/kg. {**R-154**}

*Goats*—Area: 1.44 L/kg. {**R-81**}

*Horses*—

Apparent: 1.35 L/kg. {**R-96**}

Area: 0.67 L/kg. {**R-92**}

Steady state: 0.34 L/kg. {**R-92**}

*Pigs*—Area:

Adult—1.8 L/kg. {**R-83**}

Adult with pneumonia—1.53 L/kg. {**R-83**}

*Ponies*—

Area: 1.05 L/kg. {**R-92**}

Steady state: 0.47 L/kg. {**R-92**}

*Rabbits*—0.86 L/kg. {**R-86**}

*Rats*—Area: 0.79 L/kg. {**R-91**}

Tetracycline:

*Chickens*—Steady state: 0.17 L/kg. {**R-73**}

*Pigs*—Area:  $4.5 \pm 1.1$  L/kg. {**R-74**}

*Rabbits*—Area:  $1.05 \pm .88$  L/kg. {**R-72**}

**Protein binding:**

Chlortetracycline—

*Cows*: Moderate (47 to 51%). {**R-67**}

*Sheep*: Moderate (46 to 50%). {**R-67**}

Doxycycline—

*Calves*: Very high (92%). {**R-68**}

*Cats*: Very high (98%); {**R-70**} albumin binding—76%. {**R-70**}

*Dogs*: Very high (91%); {**R-70**} albumin binding—54%. {**R-70**}

*Pigs*: Very high (93%). {**R-69**}

*Sheep*: High (84 to 90%). {**R-67**}

Oxytetracycline—

*Buffalo*: Moderate (42%). {**R-87**}

*Cows*: Low (18 to 22%) {**R-67**},

*Horses and cows*: Combined results—Moderate (50%). {**R-96**}

*Pigs*, weaned, 10 weeks of age: High (75.5%). {**R-82**}

*Sheep*: Low (21 to 25%). {**R-67**}

*Trout, rainbow*: Moderate (55%). {**R-89**}

Tetracycline—

*Cows*: Low to moderate (31 to 41%). {**R-67**}

*Sheep*: Low (28 to 32%). {**R-67**}

**Biotransformation:** *All species*—The tetracyclines are not known to be biotransformed to any significant extent before elimination. {**R-28; 68-70**}

**Half-life:** Elimination—

Chlortetracycline:

*Calves*, ruminant—8.3 hours. {**R-76**}

*Turkeys*—0.88 hour. {**R-78**}

Doxycycline:

*Calves*—

Preruminant: 9.8 hours. {**R-68**}

Ruminant: 14.2 hours. {R-68}  
 Cats—4.6 hours. {R-70}  
 Chickens—4.8 hours. {R-64}  
 Dogs—7 to 10.4 hours. {R-63; 70}  
 Horses—Oral administration (apparent half-life): 8.7 ± 1.6 hours {R-131}.  
 Pigs—3.9 hours. {R-69}

Oxytet racycline:  
 Buffalo—2.8 to 3.6 hours. {R-87}  
 Calves—  
 Newborn: 11.2 hours. {R-93}  
 6 weeks of age: 3.5 to 7.2 hours. {R-93; 100; 106}  
 6 weeks of age with induced *Mannheimia (Pasteurella) haemolytica* pneumonia: 2.5 hours. {R-106}  
 8 months of age: 6.3 hours. {R-93}

Camels—7.7 hours. {R-88}  
 Catfish, African—80.3 hours. {R-90}  
 Cows—10 hours. {R-95}  
 Dogs—6 hours. {R-84}  
 Donkeys—6.5 hours. {R-92}  
 Foals—6.7 to 7.3 hours. {R-154}  
 Goats—6.5 hours. {R-81}  
 Horses—13 hours {R-92}; 15.7 hours {R-175}.  
 Pigs—  
 10 weeks of age, weaned: 11.6 to 17.2 hours. {R-82}  
 Adult: 3.8 to 6.7 hours. {R-77; 83}  
 Adult, with pneumonia: 5.1 to 5.2 hours. {R-83}

Ponies—15 hours. {R-92}  
 Rabbits—1.3 hours. {R-86}  
 Trout, rainbow—  
*Oncorhynchus mykiss*: 60.3 hours. {R-89}  
*Salmo gairdneri*: 89.5 hours. {R-90}

Turkeys—0.73 hour. {R-85}

Tetracycline:  
 Cats—2.5 hours. {R-75}  
 Chickens—2.8 hours. {R-73}  
 Dogs—1.6 to 2 hours. {R-75}  
 Pigs—16 hours. {R-74}  
 Rabbits—2 hours. {R-72}

**Time to peak concentration/Peak serum concentration:**

Chlortetracycline—Oral:  
 Calves (22 mg/kg dose)—  
 Milk fed: 15.7 ± 0.33 hours to a peak serum concentration of 1.86 ± 0.54 mcg per mL (mcg/mL). {R-76}  
 Ruminant: 13.3 ± 2.67 hours to a peak serum concentration of 0.67 ± 0.24 mcg/mL. {R-76}  
 Turkeys—2.5 hours to a peak serum concentration of 0.6 mcg/mL (15 mg/kg dose). {R-80}

Doxycycline—Oral:  
 Single dose—  
 Chickens—0.35 ± 0.02 hour to a peak serum concentration of 54.6 ± 2.4 mcg/mL (20 mg/kg dose). {R-64}  
 Horses—  
 1 hour to a peak serum concentration of 0.22 mcg/mL (3 mg/kg dose) {R-131}.  
 1 hour to a peak serum concentration of 0.32 mcg/mL (dose of 10 mg/kg) {R-131}.  
 Multiple dosing: Horses—2 hours postadministration to a serum concentration of 0.42 mcg/mL at 2 hours after the fifth dose (five intragastric doses of 10 mg/kg administered at twelve hour intervals) {R-131}.  
 Note: The MIC<sub>90</sub> of doxycycline has been reported as =1 mcg/mL for *Streptococcus zooepidemicus* and 0.25 mcg/mL for *Staphylococcus aureus* in horses {R-131}.

Oxytetracycline—  
 Oral: Pigs, weaned, 10 weeks of age—  
 30 hours after start of administration to a peak serum concentration of 0.2 ± 0.06 mcg/mL (dose of 400 parts per million in feed for 3 days). {R-82}

1 to 5 hours to a peak serum concentration of 1.18 to 1.41 mcg/mL (20 mg per kg single dose).

**Intramuscular:**

**Conventional formulation—**

*Calves*, 14 weeks of age: 6 hours to a peak serum concentration of  $5.5 \pm 1.25$  mcg/mL (dose of 18 mg/kg in the neck). **{R-95}**

*Catfish, African*: 7 hours to a peak serum concentration of 43.4 mcg/mL (60 mg/kg dose). **{R-90}**

*Cows*: 6.7 hours to a peak serum concentration of  $5.7 \pm 2.39$  mcg/mL (dose of 8 mg/kg in the neck). **{R-95}**

*Pigs*: 1.5 hours to a peak serum concentration of  $6.7 \pm 3.4$  (dose of 20 mg/kg in the hindquarter). **{R-107}**

*Trout, rainbow*: 4 hours to a peak serum concentration of 56.9 mcg/mL (60 mg/kg dose). **{R-90}**

**Long-acting formulation—**

*Calves*, nonruminating, 5 weeks of age: 1 to 1.5 hours to a peak serum concentration of 4 mcg/mL (dose of 20 mg/kg in the gluteal muscles). **{R-99}**

*Calves*, nonruminating, 6 weeks of age:  $4.01 \pm 2.84$  hours to a peak serum concentration of  $3.01 \pm 0.72$  mcg/mL (dose of 10 mg/kg in the hindquarter). **{R-100}**

*Calves*, ruminating:  $7.6 \pm 4$  hours to a peak serum concentration of  $9.6 \pm 2.6$  mcg/mL (dose of 40 mg/kg in the hindquarter). **{R-101}**

*Camels*:  $7.3 \pm 3.5$  hours to a peak serum concentration of  $3.49 \pm 0.44$  mcg/mL (10 mg/kg dose). **{R-88}**

*Cows*: 5 to 10 hours to a peak serum concentration of 4.5 to 6.8 mcg/mL (dose of 10 mg/kg in the neck). **{R-97}**

*Pigs*: 0.5 hour to a peak serum concentration of  $6 \pm 2.2$  mcg/mL (dose of 20 mg/kg in the hindquarters). **{R-107}**

*Steers*: 8 hours to a peak serum concentration of 3.13 mcg/mL (dose of 20 mg/kg in the hindquarters). **{R-98}**

**Tetracycline—Oral: Pigs—**72 hours to a peak serum concentration of 0.6 mcg/mL (dose of 0.55 gram per kg of feed). **{R-74}**

**Duration of action:**

Note: Duration of action may be estimated by the time target serum concentrations are maintained. Target concentrations are generally based on minimum inhibitory concentrations (MIC) for each organism. While 0.5 mcg/mL has been considered the MIC of oxytetracycline for many pathogens in the past and research studies were based on that target, there are now many pathogens with MICs of 4 to 16 mcg/mL. Duration of action may be minimal or nonexistent for these isolates.

**Chlortetracycline—**

*Pigs*: When administered 110 mg chlortetracycline per kg of feed, fed as the only ration, therapeutic plasma or tissue concentrations were not produced **{R-155}**.

*Turkeys*: A single oral dose of 15 mg/kg produces serum concentrations above 0.4 mcg/mL for 8 to 10 hours. **{R-80}**

**Doxycycline—Dogs:** An intravenous dose of 5 mg/kg produces serum concentrations above 2 mcg/mL for 8 hours. **{R-63}**

**Oxytetracycline—**

**Oral:**

*Pigs*—A single oral 50 mg/kg dose produces >0.5 mcg/mL serum concentrations for at least 8 hours. **{R-109}**

*Pigs*, after challenge with *Actinobacillus pleuropneumonia*—A single oral 50 mg/kg dose produces >0.5 mcg/mL serum concentrations for at least 24 hours. **{R-109}**

*Pigs*—When administered 550 mg of oxytetracycline per kg of feed, fed as the only diet, plasma concentrations peaked at 0.4 mcg/mL **{R-107}**.

Note: These results may vary by size of pig and amount of feed intake.

**Intramuscular:**

Conventional formulation—

*Calves:* A single dose of 18 mg/kg maintains serum concentrations > 1 mcg/mL for at least 32 hours. {**R-94**}

*Cows:* A single dose of 20 mg/kg in the hindquarters maintains serum concentrations of > 0.5 mcg/mL for 52 hours {**R-98**}.

*Pigs:* A single dose of 20 mg/kg maintains serum concentrations > 0.5 mcg/mL for 28 to 36 hours. {**R-107; 174**}

Long-acting formulation—

*Calves, milk fed:* A single dose of 10 mg/kg maintains serum concentrations > 0.5 mcg/mL for 12 to 24 hours. {**R-100**}

*Calves, ruminating:* A single dose of 40 mg/kg maintains serum concentrations > 2 mcg/mL for 48 hours; {**R-101**} also lung concentrations produced are 2 mcg/mL at 48 hours. {**R-101**}

*Camels:* A single dose of 10 mg/kg maintains serum concentrations > 0.5 mcg/mL for 72 hours. {**R-88**}

*Cows:*

A single dose of 10 mg/kg in the neck maintains > 0.5 mcg/mL serum concentrations for 48 to 70 hours and milk concentrations for 33 to 49 hours. {**R-97**}

A single dose of 20 mg/kg in the hindquarters maintains serum concentrations of > 0.5 mcg/mL for 86 hours. {**R-98**}

A single dose of 20 mg/kg in the gluteal muscles maintains serum concentrations > 4 mcg/mL for 12 hours; also lung concentrations are > 0.5 mcg/mL for 65 hours. {**R-99**}

*Pigs:* A single dose of 20 mg/kg produces serum concentrations > 0.5 mcg/mL for 35 to 48 hours {**R-107; 174**}; however, the use of the long-acting formulation does not produce significantly different plasma oxytetracycline concentrations from those produced by the conventional formulation {**R-107**}.

Tetracycline—*Pigs:* A ration containing 0.55 gram of tetracycline hydrochloride per kg of feed, fed as the only ration, produces 0.3 to 0.4 mcg/mL serum concentrations for the 96 hours that it is fed. {**R-74**}

Note: These results may vary by size of pig and amount of feed intake.

**Elimination:**

Chlortetracycline—Total clearance:

*Calves, ruminating*— $2.70 \pm 0.17$  mL per minute per kg (mL/min/kg). {**R-76**}

*Pigs, fasted*— $2.75 \pm 0.92$  mL/min/kg. {**R-77**}

*Pigs, fed*— $5.12 \pm 0.88$  mL/min/kg. {**R-77**}

*Turkeys*— $3.77 \pm 0.77$  mL/min/kg. {**R-78**}

Doxycycline—Doxycycline differs from the other tetracyclines in that a large percentage is excreted into the intestines and is inactive there. {**R-133**}

*Dogs:* 90% of a single intravenous dose is eliminated within 48 hours in nonmetabolized form. Of the 90%, 16% is eliminated in urine, <5% in the bile, and the remainder in the intestines. {**R-63**}

Total clearance:

*Calves*—

Preruminant: 2.20 mL/min/kg. {**R-68**}

Ruminant: 1.07 mL/min/kg. {**R-68**}

*Cats*— $1.09 \pm 0.21$  mL/min/kg. {**R-70**}

*Dogs*—1.7 mL/min/kg {**R-63; 70**}.

*Pigs*— $1.67 \pm 0.18$  mL/min/kg. {**R-69**}

Oxytetracycline—*Calves, cows, dogs, pigs, and turkeys:* The conventional formulation of oxytetracycline is eliminated primarily by glomerular filtration; only a small amount (1 to 2% in pigs and turkeys) is eliminated in the bile. {**R-63; 82; 85; 93**}

97}

Total clearance:

Oxytetracycline—

*Buffalo*: 1.02 to 1.45 mL/min/kg. {R-87}

*Calves*, 6 to 8 weeks of age: 1.66 to 1.88 {R-93}; 2.67 to 4.67 mL/min/kg. {R-100}

*Camels*: 1.26 mL/min/kg. {R-88}

*Dogs*:  $4.23 \pm 1.29$  mL/min/kg. {R-84}

*Donkeys*: 1.52 mL/min/kg. {R-92}

*Foals*, 4 to 5 days of age: 3.17 mL/min/kg {R-154}.

*Goats*: 2.67 mL/min/kg. {R-81}

*Horses*: 0.66 mL/min/kg. {R-92}

*Pigs*, 10 weeks of age: 4.17 mL/min/kg. {R-82}

*Pigs*, adult: 3.5 mL/min/kg. {R-83}

*Ponies*: 1.01 mL/min/kg. {R-92}

*Rabbits*: 7.23 mL/min/kg. {R-86}

*Rats*: 2.79 mL/min/kg. {R-91}

Tetracycline—Total clearance:

*Chickens*— $1.63 \pm 0.18$  mL/min/kg. {R-73}

*Pigs*— $3.08 \pm 0.4$  mL/min/kg. {R-74}

*Rabbits*— $6.1 \pm 0.6$  mL/min/kg. {R-72}

## Precautions to Consider

### Species sensitivity

*All species*: Rapid intravenous administration of tetracyclines can result in cardiovascular dysfunction and collapse in any species {R-33-35; 169}. Some studies have linked the cardiovascular effects of intravenous administration in calves to the propylene glycol vehicle in some preparations {R-33; 170}; however, adverse cardiovascular effects and collapse have been shown to occur after intravenous administration of tetracycline without propylene glycol vehicle {R-34}; the electrocardiographic abnormalities may be due to chelation of free calcium ions {R-34}. Tetracyclines ideally should be diluted in fluids and administered slowly if given by the intravenous route {R-176}. If this is not possible, intravenous injections should be made as a slow push, with the dose administered over 1 to 2 minutes.

*Horses*: While rapid intravenous administration of tetracyclines causes reactions in many species, doxycycline in particular can lead to severe cardiovascular dysfunction and death when administered intravenously at any rate to horses. {R-35}

Administration of tetracyclines can also lead to severe diarrhea in some horses. However, oral, multiple-dose administration of doxycycline to horses without observed side effects has been reported {R-131}.

### Pregnancy/Reproduction

Tetracyclines have been shown to cross the placenta {R-22} and may affect fetal bone formation. {R-135}

### Lactation

Tetracyclines are distributed into milk.

### Pediatrics

Use of tetracyclines during tooth development (the last 2 to 3 weeks of pregnancy to 1 month of age) {R-22} may cause discoloration of the bones and teeth {R-4}. In neonates that have not yet developed full renal function, excretion of chlortetracycline, oxytetracycline, and tetracycline may occur more slowly than in a mature animal. One exception is that 4-day-old foals have a faster elimination half-life and more rapid clearance of oxytetracycline compared to adults {R-154}.

### Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Although methoxyflurane has been suspected of increasing the potential for tetracycline-induced nephrotoxicity in people, this has not been shown to be true in dogs. {R-137}

Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

- » Antacids or
- » Calcium supplements, such as calcium carbonate, or
- » Iron supplements or
- » Magnesium-containing laxatives or Sodium bicarbonate  
(concurrent use with tetracyclines may result in formation of non-absorbable complexes; also, concurrent use within 1 to 3 hours of antacid or sodium bicarbonate administration may result in decreased absorption of oral tetracyclines because of increased intragastric pH)
- Phenobarbital or  
Microsomal enzyme inducers, other  
(concurrent use with doxycycline may result in decreased doxycycline serum concentrations due to induction of microsomal enzyme activity; adjustment of doxycycline dosage or substitution of another tetracycline may be necessary)
- Tereftalic acid  
(blood concentrations of chlortetracycline are increased when it is administered concurrently with tereftalic acid {R-156})

#### **Human drug interactions and/or related problems{R-132}**

In addition to the above drug interactions reported in animals, the following drug interactions have been reported in humans, and are included in the human monograph *Tetracyclines (Systemic)* in *USP DI Volume I*; these drug interactions are intended for informational purposes only and may or may not be applicable to the use of tetracyclines in the treatment of animals:

- Cholestyramine  
(concurrent use with cholestyramine may result in binding of oral tetracyclines, thus impairing their absorption; an interval of several hours between administration of cholestyramine and oral tetracyclines is recommended)
- Vitamin A  
(concurrent use with tetracycline has been reported to cause benign intracranial hypertension)

#### **Laboratory value alterations**

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

With physiology/laboratory test values

- Urinalysis  
(transient hemoglobinuria has been reported in cattle given parenteral oxytetracycline) {R-38; 45; 56}

#### **Human laboratory value alterations{R-132}**

The following laboratory value alterations have been reported in humans, and are included in the human monograph *Tetracyclines (Systemic)* in *USP DI Volume I*; these laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of tetracyclines in the treatment of animals:

- With diagnostic test results
  - Catecholamine determinations, urine  
(may produce false elevations of urinary catecholamines because of interfering fluorescence)
- With physiology/laboratory test values
  - Alanine aminotransferase (ALT [SGPT]) and Alkaline phosphatase and Amylase and Aspartate aminotransferase (AST [SGOT]) and Bilirubin  
(serum concentrations may be increased)
  - Blood urea nitrogen (BUN)  
(antianabolic effect of tetracyclines [except doxycycline] may increase BUN concentrations; in patients with significantly impaired renal function, increased serum concentrations of tetracyclines may lead to azotemia, hyperphosphatemia, and

acidosis)

### Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

#### **Risk-benefit should be considered when the following medical problem exists:**

Renal function impairment, severe  
(chlortetracycline, oxytetracycline, and tetracycline are eliminated primarily by the kidney and can accumulate in animals with severe renal dysfunction; doxycycline is only partially eliminated renally and is much less likely to accumulate **{R-71}**)

#### **Patient monitoring**

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):

Culture and susceptibility, *in vitro*, and  
Minimum inhibitory concentration (MIC)  
(*in vitro* cultures and MIC test should be done on samples collected prior to administration of tetracyclines to determine pathogen susceptibility)

### Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

#### **Those indicating need for medical attention**

Incidence rare

*All species*

**Hypersensitivity reactions, specifically anaphylaxis {R-32; 45}**

(defecation; eruption of skin plaques; frothing from the mouth; glassy-eyed appearance; labored breathing; muscle trembling; piloerection; prostration; restlessness; swelling of eyelids, ears, muzzle, anus, vulva or scrotum and sheath) **{R-45}**;

**photosensitization {R-39}**

*Cattle, dogs, and horses*

**Nephrotoxicosis {R-29-31; 112; 168}**—with high doses, concurrent debilitating conditions, or use of outdated tetracyclines

Incidence unknown

*All species*

**Overgrowth of nonsusceptible organisms**

*Cats, cattle, dogs, horses, monkeys, rabbits, rats, and sheep {R-33-35}*

**Cardiovascular dysfunction, including atrioventricular block, atrial tachycardia, ventricular bradycardia, hypotension** (in order of appearance—agitation or nervousness, dyspnea, muscle fasciculations, urination, defecation, collapse, death)—a dose-dependent effect **{R-34}** with rapid intravenous administration; **cardiovascular dysfunction, including hypertension, arterial {R-35}**—in horses given doxycycline

Note: Although the propylene glycol vehicle of some oxytetracycline preparations has been shown to have some cardiovascular effects when administered intravenously **{R-33}**, the calcium-binding nature of the tetracyclines has been implicated in *cardiovascular dysfunction* and sudden collapse in cattle and sheep after intravenous administration of tetracyclines. **{R-34; 35}** Although pretreatment with calcium borogluconate has been considered before intravenous administration **{R-34}**, specific postreaction therapy for possible hypocalcemia has not been recommended.

In horses, doses of doxycycline as low as 0.2 to 0.4 mg per kg of body weight administered intravenously have caused *cardiovascular dysfunction*, collapse, and death. Instead of hypotension, *hypertension* is reported in horses given intravenous doxycycline and is associated with the other signs

of cardiovascular dysfunction seen with rapid intravenous tetracycline administration in other species.

*Cats*

**Fever** (anorexia, sometimes diarrhea)—usually resolves within 48 hours of discontinuing oxytetracycline or tetracycline {**R-39**}

*Cattle*

**Hemoglobinuria, transient** {**R-38; 45; 56**} (brownish -red urine)—with parenteral administration of oxytetracycline; **hepatitis with fatty degeneration and/or bile stasis** {**R-168**}—with repeated high doses or concurrent debilitating conditions

*Horses*

**Colitis; diarrhea, severe**

*Psittacine birds (cockatoos, macaws, and parrots)*

**Aspergillosis, increased risk of**—may occur with prolonged chlortetracycline treatment {**R-152**}

*Rabbits*

**Anorexia; diarrhea**—with doses administered that are two times the recommended dose {**R-86**}

**Those indicating need for medical attention only if they continue or are bothersome**

Incidence more frequent

*All species*

**Discoloration of teeth in young animals** (yellow, brown, or grey discoloration)—when administered during late pregnancy or during period of tooth development {**R-39**}; **local tissue irritation at site of injection**—with intramuscular administration {**R-37; 101**}

*Cats and dogs*

**Nausea or vomiting**—with oral administration {**R-39**}, in particular, with doxycycline on an empty stomach {**R-156**}

**Human side/adverse effects {R-132}**

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph *Tetracyclines (Systemic)* in *USP DI Volume I*; these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of tetracyclines in the treatment of animals:

Incidence more frequent

**Central nervous system toxicity; staining of infants' or children's teeth; gastrointestinal disturbances; photosensitivity**

Incidence less frequent

**Fungal overgrowth; hypertrophy of the papillae; nephrogenic diabetes insipidus; pigmentation of skin and mucous membranes**

Incidence rare

**Benign intracranial hypertension; hepatotoxicity; pancreatitis**

Note: Tetracycline-induced *hepatotoxicity* is usually seen as a fatty degeneration of the liver. It is more likely to occur in pregnant women, in patients receiving high-dose intravenous therapy, and in patients with renal function impairment. However, hepatotoxicity has also occurred in patients without these predisposing conditions.

Tetracycline-induced *pancreatitis* has also been described in association with hepatotoxicity, and without associated liver disease.

## Overdose

For more information in cases of overdose or unintentional ingestion,

**contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

Overdose of tetracyclines in animals is unusual because very high doses are often tolerated; however, effects that have been associated with overdose in animals include nephrotoxicosis and possible hepatotoxicity.

Acute toxicity of intravenously-administered tetracyclines {**R-33; 34**} in many species is most often seen with rapid administration; however,

intravenous doxycycline administration in horses has caused collapse even when administered over a 3- to 7-minute period. This reaction to intravenous tetracyclines is dose-dependent, but is not only associated with high doses.

Administration of repeated high doses of intravenous or intramuscular oxytetracycline to calves or cattle can result in renal cortical tubular nephrosis. While a single intramuscular dose of 40 mg of an oxytetracycline per kg (in a 2-pyrrolidine formulation) administered to healthy calves produced no significant toxicity {R-101}, studies have shown that 33 to 44 mg of oxytetracycline per kg of body weight a day administered intravenously or intramuscularly for 2 or more days can produce renal protein casts, tubular necrosis, and death in calves with respiratory disease {R-30; 168}. A similar dose of 33 mg oxytetracycline per kg of body weight administered intravenously for 3 days produces a rise in blood urea nitrogen and the appearance of renal casts in the urine of normal heifers {R-167}. The vehicles used in formulations, such as propylene glycol, have been linked to reduced renal blood flow and have been suspected of exacerbating adverse effects {R-29; 33}. Tetracycline and its degradation products have been reported to also cause nephrotoxicity in cattle and foals {R-29; 112}. Serious toxicity can be expected to be more likely in animals that are already compromised by disease or dehydration.

Hepatotoxicity has been reported as a human side effect of tetracyclines and may be more common in pregnant women {R-167}. Hepatic fatty degeneration has been observed in people and has been induced in mice and rats given extremely high doses (100 to 300 mg of tetracycline per kg of body weight); however, fatty infiltration of the liver was also observed in calves that had respiratory disease and that developed renal tubular necrosis after administration of two doses of 33 mg of oxytetracycline per kg of body weight 24 hours apart {R-168}.

## Veterinary Dosing Information

### For oral dosage forms only

For some tetracyclines, serum concentrations from animal to animal vary more widely when administered in drinking water than when administered in feed. {R-59}

Unlike other tetracyclines, doxycycline can be used without dosage adjustment in animals with renal function impairment.

### For parenteral dosage forms only

Care should be taken to administer intravenous tetracyclines slowly and/or dilute them in fluids to avoid cardiovascular side effects. {R-33-35}

Intramuscular injection of oxytetracycline will affect the quality of meat for a prolonged period. Whenever possible, subcutaneous administration should be chosen {R-65}.

### Diet/Nutrition

Oral tetracyclines are absorbed more efficiently when administered without food, particularly without foods containing divalent or trivalent metals, such as milk or milk replacer. Doxycycline absorption appears to be less affected than other tetracyclines.

### For treatment of adverse effects

Recommended treatment consists of the following:

#### *For anaphylaxis*

- Parenteral epinephrine.
- Oxygen administration and respiratory support.

### For treatment of acute reactions to intravenous administration

Recommended treatment consists of the following:

- Intravenous fluids.
- Oxygen administration and respiratory support.

Note: Because the specific causes of acute reactions may be difficult to immediately determine, an electrocardiogram should be monitored when possible to identify cardiac arrhythmias and direct the course of therapy.

## CHLORTETRACYCLINE

### Additional Dosing Information

When possible, oral chlortetracycline should be administered 1 hour before or 2 hours after milk replacer. **{R-1}**

### Mucosal Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### CHLORTETRACYCLINE UTERINE TABLETS

#### Usual dose:

Note: [*Cattle*]<sup>1</sup>—Although the efficacy and safety are not currently established, an intrauterine dose of 500 to 1000 mg administered as a single dose after parturition **{R-118}** for the treatment of *acute uterine infections* is included in Canadian product labeling. [*Ewes*] and [*sows*]<sup>1</sup>—Although the efficacy and safety are not currently established, an intrauterine dose of 250 to 500 mg administered as a single dose after parturition **{R-118}** for the treatment of *acute uterine infections* is included in Canadian product labeling.

#### Strength(s) usually available **{R-58}**:

U.S.—

Veterinary-labeled products:  
Not commercially available.

Canada—

Veterinary-labeled products:  
500 mg (OTC) [*Aureomycin Uterine Oblets*].

#### Withdrawal times:

Canada—

Species	Withdrawal time
	Meat (days)
<i>Cattle, pigs, sheep</i>	0

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

**USP requirements:** Not in USP.

### Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### CHLORTETRACYCLINE HYDROCHLORIDE SOLUBLE POWDER USP

#### Usual dose:

*Calves*<sup>1</sup> and *pigs*<sup>1</sup>—

Bacterial enteritis; or  
Bacterial pneumonia: Oral, 22 mg per kg of body weight a day, administered in the only source of drinking water. **{R-17}**

*Chickens*<sup>1</sup>—

Chronic respiratory disease: Oral, 400 to 800 mg per gallon of water **{R-17}** (approximately 22 to 59 mg per kg of body weight a day **{R-143}**), administered in the only source of drinking water. **{R-17}**

Fowl cholera: Oral, 1000 mg (1 gram) per gallon of water, administered in the only source of drinking water. **{R-17}**

Synovitis: Oral, 200 to 400 mg per gallon of water (approximately 11 to 29.5 mg per kg of body weight a day),

administered in the only source of drinking water. {R-17; 143}

*Turkeys, growing*<sup>1</sup>—

Enteritis: Oral, 55 mg per kg of body weight a day, administered in the only source of drinking water. {R-17}

Infectious synovitis: Oral, 400 mg per gallon of water (approximately 7 to 37 mg per kg of body weight a day), administered in the only source of drinking water. {R-143}

Note: Environmental and health conditions may affect the intake of water and the amount of medication consumed. {R-17}

Administration of medication in food or water to animals with pneumonia or other infections can be affected by reduced feed and water intake {R-109}.

**Strength(s) usually available {R-58}:**

U.S.— {R-17}

Veterinary-labeled products:

25 grams per pound of powder (OTC) [*Aureomycin Soluble Powder*].

64 grams per pound of powder (OTC) [*AmTech Chlortetracycline HCL Soluble Powder; Aureomycin Soluble Powder Concentrate; CTC Soluble Powder Concentrate; Pennchlor 64 Soluble Powder*].

Canada—

Veterinary-labeled products:

Not commercially available.

**Withdrawal times:**

Note: With chlortetracycline soluble powder, withdrawal times vary greatly from product to product and may differ from those listed below. See also individual manufacturer's labeling.

U.S.— {R-17; 58}

Species	Withdrawal time
	Meat (days)
<i>Calves, chickens, and turkeys</i>	1
<i>Pigs</i>	1 or 5, depending on product

Note: Product labeling with the above withdrawal time listed for poultry states that it applies when the medication is mixed at 1000 mg of chlortetracycline per gallon of drinking water. Product labeling with the above withdrawal times states that they apply when cattle and pigs are treated for a maximum of five days and chickens and turkeys are treated for a maximum of fourteen days. Not labeled for use in laying hens, preruminating calves, or lactating dairy cattle.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer. Protect from light.

**Preparation of dosage form:** Fresh solutions should be prepared every 24 hours. When administered in a galvanized waterer, fresh solutions should be prepared every 12 hours.

**Incompatibilities:** Administration 1 hour before or 2 hours after giving milk or milk replacers is recommended. Chlortetracycline hydrochloride soluble powder should not be mixed with milk replacers.

**USP requirements:** Preserve in tight containers, protected from light. Label it to indicate that it is intended for oral veterinary use only. Contains the labeled amount, within -10% to +25%. Meets the requirement for Loss on drying (not more than 2.0%). {R-128}

**CHLORTETRACYCLINE FOR MEDICATED FEED**

**Usual dose:**

*Calves—*

Improved feed efficiency and increased weight gain for calves weighing up to 250 pounds<sup>1</sup>: Oral, 0.22 mg per kg of body weight a day administered in the feed, fed as the only ration. **{R-16; 152}**

Improved feed efficiency and increased weight gain for calves weighing 250 to 400 pounds<sup>1</sup>: Oral, 25 to 70 mg per animal a day administered in the feed, fed as the only ration. **{R-16; 152}**

Enteritis: Oral, 22 mg per kg of body weight a day, administered in the feed and fed as the only ration **{R-152}**.

Note: Products made to add to calf milk replacer are indicated for treatment of bacterial enteritis and for improved feed efficiency and increased weight gain only.

*Cattle—*

Anaplasmosis (treatment)<sup>1</sup>:

Cattle weighing < 700 pounds—Oral, 350 mg per animal a day, administered in the feed and fed as the only ration **{R-16; 152}**.

Cattle weighing = 700 pounds—Oral 1.1 mg per kg of body weight a day, administered in the feed and fed as the only ration **{R-152}**.

Bacterial enteritis<sup>1</sup>; or bacterial pneumonia (treatment)<sup>1</sup>: Oral, 22 mg per kg of body weight a day, administered in the feed and fed as the only ration **{R-152}**.

Bacterial pneumonia (control)<sup>1</sup>: Oral, 350 mg per animal a day administered in the feed, fed as the only ration. **{R-16; 152}**

Improved feed efficiency and increased rate of weight gain<sup>1</sup>; or hepatic abscesses (prophylaxis)<sup>1</sup>: Oral, 70 mg a day per animal administered in the feed, fed as the only ration. **{R-16; 152}**

[Pododermatitis (prophylaxis)]: Oral, 0.22 mg per kg of body weight a day or 70 mg per animal a day, administered in the feed and fed as the only ration **{R-116}**.

*Chickens—*

Chronic respiratory disease: Oral, 200 to 400 grams per ton of feed, fed as the only ration. **{R-16; 152}**

*Escherichia coli* infections<sup>1</sup>: Oral, 500 grams per ton of feed, fed as the only ration. **{R-16; 115}**

Improved feed efficiency and increased rate of weight gain: Oral, 10 to 50 grams per ton of feed, fed as the only ration. **{R-152}**

Synovitis<sup>1</sup>: Oral, 100 to 200 grams per ton of feed, fed as the only ration **{R-152}**.

[Enteritis; or increased egg production or hatchability]: Oral, 100 to 200 grams per ton of feed (110 to 220 grams per metric ton [1000 kg] of feed), fed as the only ration.

Note: Canadian product labeling also lists the above dose for feed efficiency.

*Cockatoos, macaws, and parrots—Psittacosis*<sup>1</sup>: Oral, 10 mg per gram of mash or feed, administered continuously for 45 days as the only ration **{R-152}**.

*Ducks*<sup>1</sup>—Fowl cholera: Oral, 200 to 400 grams per ton of feed (approximately 17.6 to 61.6 mg per kg of body weight a day) administered in the feed, fed as the only ration. **{R-16; 152}**

*Pigs—*

Cervical abscesses (prophylaxis)<sup>1</sup>: Oral, 50 to 100 grams per ton of feed, fed as the only ration. **{R-115}**

Bacterial enteritis; or bacterial pneumonia<sup>1</sup>: Oral, 22 mg per kg of body weight a day, administered in the only ration **{R-152}**.

Improved feed efficiency and increased rate of weight gain: Oral, 10 to 50 grams per ton of feed, fed as the only ration. **{R-152}**

For reducing the shedding of leptospirosis and the incidence of associated abortion<sup>1</sup>: Oral, 400 grams per ton of feed, fed as the only ration for fourteen days. **{R-152}**

Note: Canadian product labeling lists a dose in the treatment of enteritis and for increasing feed efficiency and improving weight gain of 50 to 100 grams per ton of feed (55 to 110

grams per metric ton [1000 kg] of feed), fed as the only ration **{R-116}**.

*Sheep*—Vibronic abortion (prophylaxis)<sup>1</sup>: Oral, 80 mg per animal a day administered in the feed, fed as the only ration continuously during pregnancy. **{R-16; 152}**

*Sheep*, growing—Improved feed efficiency and increased rate of weight gain<sup>1</sup>: Oral, 20 to 50 grams per ton of feed, fed as the only ration. **{R-16}**

*Turkeys*—

Bacterial enteritis: Oral, 55 mg per kg of body weight a day, administered in the only ration **{R-16; 152}**.

Note: Canadian product labeling lists a dose in the treatment of enteritis of 100 to 200 grams per ton of feed (110 to 220 grams per metric ton [1000 kg] of feed), fed as the only ration **{R-116}**.

Hexamitiasis<sup>1</sup>: Oral, 400 grams per ton of feed, fed as the only ration **{R-16; 152}**.

Synovitis<sup>1</sup>: Oral, 200 grams per ton of feed, fed as the only ration **{R-16; 152}**.

[Increased egg production; or sinusitis (prophylaxis)]: Oral, 100 to 200 grams per ton of feed (110 to 220 grams per metric ton [1000 kg] of feed), fed as the only ration.

*Turkeys*, growing, less than 4 weeks of age—Paratyphoid<sup>1</sup>: Oral, 400 grams per ton of feed, fed as the only ration. **{R-115}**

*Turkeys*, growing—Improved efficiency or; increased rate of weight gain: Oral 10 to 50 grams per ton of feed, fed as the only ration **{R-16; 152}**.

[*Lambs*]—Enterotoxemia: Oral, 20 grams per ton of feed (22 grams per metric ton [1000 kg] of feed), fed as the only ration.

Note: Environmental and health conditions may affect the intake of water and the amount of medication consumed. **{R-17}**

Administration of medication in food or water to animals with pneumonia or other infections can be affected by reduced feed and water intake **{R-109}**.

**Strength(s) usually available {R-58}:**

U.S.—

Veterinary-labeled products:

110 grams per kg of premix (OTC) [*Aureomycin 50 Granular; ChlorMax 50; CTC 50; Pennchlor 50•G; Pennchlor 50 Meal*].

154 grams per kg of premix (OTC) [*Pennchlor 70 Meal*].

198 grams per kg of premix (OTC) [*Aureomycin 90 Granular; Pennchlor 90•G*].

220 grams per kg of premix (OTC) [*Aureomycin 100 Granular; CLTC 100 MR; Pennchlor 100 Hi-Flo Meal; Pennchlor 100MR*].

Canada—

Veterinary-labeled products:

110 grams per kg of premix (OTC) [*Aureomycin 110G; Chlor 50; Chlorosol-50*].

220 grams per kg of premix (OTC) [*Aureomycin 220G; Chlor 100*].

**Withdrawal times {R-58}:**

Note: With chlortetracycline oral premix, withdrawal times vary greatly from product to product and may differ from those listed below. See also individual manufacturer's labeling.

U.S.— **{R-123}**

Species	Withdrawal time	
	Meat (days)	Eggs (hours)
<i>Calves, cattle</i>	0, 1, or 2, depending on product and dose	
<i>Chickens</i>	0 or 1, depending on product and dose	0 for some products
<i>Pigs, sheep, turkeys</i>	0	

Note: Product labeling listing the above withdrawal times states that

they apply when product is fed to calves at a dose of up to 70 mg per animal a day, and to cattle at a dose of 350 mg per animal a day or 1.1 mg per kg of body weight a day in feed, to chickens at 500 grams or more per ton of feed for a maximum of five days, to pigs at 400 grams or less per ton of feed or 22 mg per kg of body weight a day for up to fourteen days, and to sheep when fed 80 mg per animal a day or 20 to 50 grams per ton of feed.

Not labeled for use in preruminating calves, lactating dairy cows, or horses to be used for food. **{R-16}**

Some products are not labeled for use in chickens, ducks, or turkeys producing eggs for human consumption. **{R-152}**

When fed at 22 mg per kg of body weight a day:

Species	Withdrawal time
	Meat (days)
<i>Calves, cattle</i>	0 or 10, depending on product

Note: Not labeled for use in lactating dairy cows. **{R-16}**

Canada—

Species	Withdrawal time
	Meat (days)
<i>Calves, cattle</i>	5
<i>Chickens, pigs, turkeys</i>	7
<i>Lambs</i>	4

Note: Product labeling listing the above withdrawal times states that they apply when the product is fed to chickens and turkeys at 55 to 220 mg per kg of feed, to pigs at 55 to 110 mg per kg of feed, to calves at 55 mg per kg of feed, to lambs at 22 mg per kg of feed, and to cattle at 0.22 mg per kg of body weight or 70 mg per animal.

Not labeled for use in lactating dairy cows.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

**USP requirements:** Not in USP.

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## DOXYCYCLINE

### Summary of Differences

Pharmacology/pharmacokinetics: More completely absorbed from the gastrointestinal tract than the tetracyclines developed earlier and absorption is less likely to be affected by food or calcium or other divalent or trivalent metals. Doxycycline is also more lipid-soluble than other tetracyclines. In dogs, doxycycline is eliminated primarily through intestinal excretion. **{R-63}**

Precautions: Medical considerations—Doxycycline is only partially eliminated renally and is less likely to accumulate in animals with renal function impairment; it can be used without dosage adjustment.

Side/adverse effects: *Horses*—Intravenous administration can lead to cardiovascular dysfunction and death. **{R-34}**

### Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

The dosing and strengths of the dosage forms available are

expressed in terms of doxycycline base.

### DOXYCYCLINE FOR ORAL SUSPENSION USP

**Usual dose:** [Rocky Mountain spotted fever]<sup>1</sup>—*Dogs*: Oral, 5 mg per kg of body weight every twelve hours **{R-151}** for fourteen days.

Note: [*Cats*]<sup>1</sup>—Although the efficacy has not been established, an oral dose of 5 mg per kg of body weight every twelve hours for twenty-one days has been used in the treatment of *feline infectious anemia* **{R-147; 151}**. For *chlamydial infections* or *respiratory infections* in cats, a dose of 5 mg per kg of body weight every twelve hours or 10 mg per kg of body weight every twenty-four hours has been used **{R-151}**.

[*Dogs*]<sup>1</sup>—Although the efficacy has not been established, an oral dose of 10 mg per kg of body weight every twelve hours for two to three weeks has been used for the treatment of *ehrlichiosis*; this regimen is based on a clinical trial that found, however, that only two out of five dogs treated with the above dose and a twenty-four-hour dosing interval for one week were cleared of *Ehrlichia canis*, as shown by negative blood and tissue cultures **{R-40}**. A dose of 5 mg per kg of body weight every twelve hours for six to eight weeks has been used in the treatment of ehrlichiosis to decrease the risk of side effects **{R-176}**; however, the efficacy of this regimen has not been confirmed. Retesting serum immunofluorescent antibody for *E. canis* two months posttreatment is recommended, and retreatment should be started if values have not dropped significantly. **{R-40}**

#### Strength(s) usually available:

U.S.—

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

5 mg (base) per mL, when reconstituted according to manufacturer's instructions (Rx) [*Vibramycin*].

Canada—

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

Not commercially available.

**Packaging and storage:** Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

**Stability:** After reconstitution, suspensions retain their potency for 14 days at room temperature.

**Auxiliary labeling:** • Shake well.

**USP requirements:** Preserve in tight, light-resistant containers.

Contains one or more suitable buffers, colors, diluents, flavors, and preservatives. Contains the labeled amount, within –10% to +25% when constituted as directed. Meets the requirements for Identification, Uniformity of dosage units (single-unit containers), Deliverable volume, pH (5.0–6.5, in the suspension constituted as directed in the labeling), and Water (not more than 3.0%). **{R-128}**

### DOXYCYCLINE CALCIUM ORAL SUSPENSION USP

**Usual dose:** See *Doxycycline for Oral Suspension USP*.

#### Strength(s) usually available:

U.S.—

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

10 mg (base) per mL (Rx) [*Vibramycin*].

Canada—

Veterinary-labeled products:  
Not commercially available.  
Human-labeled products:  
Not commercially available.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container. Protect from freezing.

**Auxiliary labeling:** • Shake well.

**USP requirements:** Preserve in tight, light-resistant containers. Prepared from Doxycycline Hyclate, and contains one or more suitable buffers, colors, diluents, flavors, and preservatives. Contains an amount of doxycycline calcium equivalent to the labeled amount of doxycycline, within –10% to +25%. Meets the requirements for Identification, Uniformity of dosage units (single-unit containers), Deliverable volume, and pH (6.5–8.0). **{R-128}**

### **DOXYCYCLINE HYCLATE CAPSULES USP**

**Usual dose:** See *Doxycycline for Oral Suspension USP*.

#### **Strength(s) usually available:**

U.S.— **{R-135}**

Veterinary-labeled products:  
Not commercially available.

Human-labeled products:  
50 mg (base) (Rx) [*Vibramycin*; GENERIC].  
100 mg (base) (Rx) [*Vibramycin*; GENERIC].

Canada—

Veterinary-labeled products:  
Not commercially available.

Human-labeled products:  
100 mg (base) (Rx) [*Alti-Doxycycline*; *Apo-Doxy*; *Doxycin*; *Doxytec* (lactose); *Novo-Doxylin*; *Nu-Doxycycline*; *Vibramycin*].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

**USP requirements:** Preserve in tight, light-resistant containers. Contain an amount of doxycycline hyclate equivalent to the labeled amount of doxycycline, within –10% to +20%. Meet the requirements for Identification, Dissolution (80% in 30 minutes in water in Apparatus 2 at 75 rpm), Uniformity of dosage units, and Water (not more than 8.5%). **{R-128}**

### **DOXYCYCLINE HYCLATE DELAYED-RELEASE CAPSULES USP**

Note: Delayed-release capsules must be swallowed whole and, in general, absorption of delayed-release dosage forms is unpredictable in animals. Doxycycline Hyclate Delayed-release Capsules USP are not recommended for use in animals.

#### **Strength(s) usually available:**

U.S.—

Veterinary-labeled products:  
Not commercially available.

Human-labeled products:  
100 mg (base) (Rx) [*Doryx* (lactose)].

Canada—

Veterinary-labeled products:  
Not commercially available.

Human-labeled products:  
Not commercially available.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

**USP requirements:** Preserve in tight, light-resistant containers. The label indicates that the contents of the Capsules are enteric-coated. Contain an amount of doxycycline hyclate equivalent to the labeled amount of doxycycline, within –10% to +20%. Meet the requirements for Identification, Drug release (Acid stage: 50% [Level 1 and Level 2] in 20 minutes in 0.06 N hydrochloric acid in Apparatus 1 at 50 rpm; Buffer stage: 85% in 30 minutes in neutralized phthalate buffer [pH 5.5] in Apparatus 1 at 50 rpm), Uniformity of dosage units, and Water (not more than 5.0%). {**R-128**}

### DOXYCYCLINE HYCLATE TABLETS USP

**Usual dose:** See *Doxycycline for Oral Suspension USP*.

#### Strength(s) usually available:

U.S.— {**R-135**}

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

100 mg (base) (Rx) [*Vibra-Tabs*; GENERIC].

Canada—

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

100 mg (base) (Rx) [*Alti-Doxycycline*; *Apo-Doxy-Tabs*; *Doxycin*; *Novo-Doxilin*; *Nu-Doxycycline*; *Vibra-Tabs*; *Vibra-Tabs C-Pak*].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

**USP requirements:** Preserve in tight, light-resistant containers. Contain an amount of doxycycline hyclate equivalent to the labeled amount of doxycycline, within –10% to +20%. Meet the requirements for Identification, Dissolution (85% in 90 minutes in water in Apparatus 2 at 75 rpm), Uniformity of dosage units, and Water (not more than 5.0%). {**R-128**}

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

### Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

The dosing and strengths of the dosage forms available are expressed in terms of doxycycline base (not the hyclate salt).

### DOXYCYCLINE FOR INJECTION USP

#### Usual dose:

Note: [*Dogs*]<sup>1</sup>—Although the efficacy has not been established, an intravenous dose of 3 to 5 mg (base) per kg of body weight every twelve hours has been used in the treatment of susceptible *bacterial infections*. {**R-70**}

This dose is based on pharmacokinetic studies.

#### Size(s) usually available:

U.S.—

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

100 mg (base) (Rx) [*Vibramycin*].

200 mg (base) (Rx) [*Vibramycin*].

Canada—

Veterinary-labeled products:

Not commercially available.

Human-labeled products:

Not commercially available.

**Packaging and storage:** Prior to reconstitution, store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light.

**Preparation of dosage form:** To prepare initial dilution for intravenous use, 10 mL of sterile water for injection or other suitable diluent (see manufacturer's package insert) should be added to each 100-mg vial or 20 mL of diluent should be added to each 200-mg vial. The resulting solution containing the equivalent of 100 to 200 mg of doxycycline may be further diluted in 100 to 1000 mL or in 200 to 2000 mL of suitable diluent, respectively.

**Stability:**

After reconstitution, intravenous infusions of doxycycline hyclate retain their potency for twelve hours at room temperature or for seventy-two hours if refrigerated at concentrations of 100 mcg (0.1 mg) to 1 mg per mL in suitable fluids (see manufacturer's package insert). Intravenous infusions of doxycycline hyclate retain their potency for six hours at room temperature at concentrations of 100 mcg (0.1 mg) to 1 mg per mL in lactated Ringer's injection or 5% dextrose and lactated Ringer's injection. Infusions must be protected from direct sunlight during administration.

If frozen immediately after reconstitution with sterile water for injection, solutions at concentrations of 10 mg per mL retain their potency for up to eight weeks at -20 °C (-4 °F). Once thawed, solutions should not be refrozen.

**Additional information:**

Concentrations of less than 100 mcg (0.1 mg) per mL or greater than 1 mg per mL are not recommended.

Infusions may be administered over a one- to four-hour period. Rapid administration should be avoided.

Intramuscular or subcutaneous administration is not recommended.

**USP requirements:** Preserve in Containers for Sterile Solids, protected from light. Contains an amount of doxycycline hyclate equivalent to the labeled amount of doxycycline, within -10% to +20%. Meets the requirements for Constituted solution, Identification, Bacterial endotoxins, Sterility, pH (1.8-3.3, in the solution constituted as directed in the labeling), Loss on drying (not more than 4.0%), and Particulate matter. **{R-128}**

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## ***OXYTETRACYCLINE***

### **Additional Dosing Information**

When possible, oral oxytetracycline should be administered 1 hour before or 2 hours after milk replacer. **{R-1}**

### **Mucosal Dosage Forms**

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### **OXYTETRACYCLINE HYDROCHLORIDE UTERINE SUSPENSION**

**Usual dose:**

Note: [*Cows*—Although the efficacy and safety are not currently established, an intrauterine dose of 3.9 to 4.4 mg per kg of body weight, administered as a single dose **{R-12}**, is included in Canadian product labeling for the treatment of *uterine infections*.

**Strength(s) usually available {R-58}:**

U.S.—

Veterinary-labeled products:  
Not commercially available.

Canada— **{R-12}**

Veterinary-labeled products:  
50 mg per mL (Rx) [*Kelamycin*].

**Withdrawal times:**

Canada—

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cows</i>	18	24

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

**Preparation of dosage form:** Warm to body temperature to ease administration. **{R-12}**

**Stability:** Preparation may darken on standing, but the potency remains unaffected. **{R-12}**

**USP requirements:** Not in USP.

**Oral Dosage Forms**

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

**OXYTETRACYCLINE HYDROCHLORIDE SOLUBLE POWDER USP**

**Usual dose:**

*Bees*—American and European foul brood: Oral, 200 mg per colony once every four to five days for three treatments in the spring and/or fall. Powder is dusted on the outer parts of the frames or mixed as a syrup and fed in feeder pails or in the combs. **{R-6; 61; 134}**

Note: Honey from infected colonies should not be used for the preparation of medicated syrup.

*Calves and cattle*—

Bacterial enteritis: Oral, 22 mg per kg of body weight every twenty-four hours, administered in the only source of drinking water or as a drench. **{R-61}**

Bacterial pneumonia<sup>1</sup>: Oral, 22 mg per kg of body weight every twenty-four hours, administered in the only source of drinking water or as a drench. **{R-61}**

*Chickens*—

Chronic respiratory disease; or fowl cholera: Oral, 400 to 800 mg per gallon of water (approximately 22 to 59 mg per kg of body weight a day), administered as the only source of drinking water. **{R-11; 121}**

Synovitis<sup>1</sup>: Oral, 200 to 400 mg per gallon of water, administered as the only source of drinking water. **{R-11; 13; 61; 121}**

[Bacterial enteritis]: Oral, 200 to 400 mg per gallon of water, administered as the only source of drinking water. **{R-61}**

*Pigs*—

Bacterial enteritis: Oral, 22 mg per kg of body weight, administered in the only source of drinking water. **{R-11; 13; 61}**

Bacterial pneumonia: Oral, 22 mg per kg of body weight, administered in the only source of drinking water **{R-6; 13}**.  
 Leptospirosis<sup>1</sup>: Oral, 22 mg per kg of body weight, administered in the only source of drinking water **{R-6; 13}**.

*Sheep*—

Bacterial enteritis: Oral, 22 mg per kg of body weight every twenty-four hours, administered in the only source of drinking water. **{R-61}**

Bacterial pneumonia<sup>1</sup>: Oral, 22 mg per kg of body weight every twenty-four hours, administered in the only source of drinking water **{R-13}**.

*Turkeys, growing*—Bacterial enteritis: Oral, 55 mg per kg of body weight a day for seven to fourteen days. **{R-7; 11; 13}**

*Turkeys*—

Hexamitiasis<sup>1</sup>: Oral, 200 to 400 mg per gallon of water (approximately 3.5 to 37 mg per kg of body weight a day), administered as the only source of drinking water. **{R-11}**

Synovitis<sup>1</sup>: Oral, 400 mg per gallon of water (7 to 37 mg per kg of body weight a day), administered as the only source of drinking water. **{R-7; 11; 13}**

Note: Environmental and health conditions may affect the intake of water and the amount of medication consumed. **{R-17}** Administration of medication by food or water to animals with pneumonia or other infections can be affected by reduced feed and water intake **{R-109}**.

**Strength(s) usually available {R-58}:**

U.S.—

Veterinary-labeled products:

- 25 grams per pound of powder (OTC) [*AmTech Oxytetracycline HCL Soluble Powder; Terramycin Soluble Powder; Terra-Vet Soluble Powder*].
- 166 grams per pound of powder (OTC) [*Oxytet Soluble; Travet-CA; Tetroxy HCA Soluble Powder*].
- 343 grams per pound of powder (OTC) [*Agrimycin -343; AmTech Oxytetracycline HCL Soluble Powder-343; Oxytet-343 Water Soluble Powder; Pennox 343 Soluble Powder; Terramycin -343 Soluble Powder; Terra-Vet Soluble Powder 343; GENERIC*].

Canada—

Veterinary-labeled products:

- 11 mg per gram of powder (OTC) [*Foul Brood Mix*].
- 55 mg per gram of powder (OTC) [*Oxytetra-A; Oxytet-25-S*].
- 62.5 mg per gram of powder (OTC) [*Oxysol-62.5; Oxytet-SP*].
- 220 mg per gram of powder (OTC) [*Oxy Tetra Forte*].
- 250 mg per gram of powder (OTC) [*Oxy 250; Oxysol-250; Oxytet-250 Concentrate*].
- 1 gram per gram of powder (OTC) [*Oxy 1000; Oxysol-1000*].

**Withdrawal times {R-58}:**

Note: With oxytetracycline soluble powder, withdrawal times vary greatly from product to product and may differ from those listed below.

See also individual manufacturer labeling.

*Bees*: To avoid contamination of honey, oxytetracycline hydrochloride soluble powder should be fed early in the spring or fall before the main honey flow begins. Honey stored during medication should be removed following last medication and cannot be used for human food. **{R-61}**

Species	Withdrawal time
	Meat (days)
<i>Calves, cattle, sheep</i>	5
<i>Chickens</i>	0
<i>Pigs</i>	0, 5, or 13, depending on product
<i>Turkeys</i>	0 or 5, depending on product

Note: Product labeling listing the above withdrawal times states

that treatment of calves, cattle, pigs, and sheep should be for a maximum of five days and chickens and turkeys for a maximum of fourteen days. Not labeled for use in lactating dairy cattle, prurminating calves, or birds producing eggs for human consumption.

Canada—{R-54}

Species	Withdrawal time	
	Meat (days)	
<i>Calves, pigs, sheep</i>	10	
<i>Chickens, turkeys</i>	7	

Note: Product labeling listing the above withdrawal times states that they apply to doses of 5 to 10 mg per kg of body weight every twelve hours for three to five days for calves, 10 mg per kg of body weight every twelve hours for three or four days for pigs, 50 mg per L of drinking water for three or four days for chickens and turkeys, and 5 mg per kg of body weight every twelve hours for three or four days for sheep. These products are not labeled for use in lactating dairy cattle or birds producing eggs for human consumption {R-54}

Species	Withdrawal time		
	Meat (days)	Milk (hours)	Eggs (hours)
<i>Cattle</i>	10	60 or 96, depending on product	
<i>Chickens, turkeys</i>	7		60 or 120, depending on product
<i>Pigs, sheep</i>	10		

Note: Some products are not labeled for use in lactating cattle and some are not labeled for use in poultry laying eggs for human consumption. Product labeling listing the above withdrawal times states that they apply to doses of 22 mg per kg of body weight a day for five days for calves and cattle, 33 mg per kg of body weight a day for pigs, and 111 mg per L of water for chickens and turkeys.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

**Preparation of dosage form:**

Oxytetracycline soluble powder can be mixed with water and administered as a drench. Fresh drinking water and drench solutions should be prepared daily as recommended by the manufacturer. {R-11; 23}

For bees, medication is mixed with powdered sugar and dusted on the frames or mixed with sugar and water to form a paste or syrup and applied as recommended by manufacturer. {R-54}

**Stability:** Stable for twenty-four hours. {R-11}

**Incompatibilities:** Milk replacer—Oxytetracycline is bound to milk replacer at a rate of 63%; this is a binding that is not readily reversible. {R-111} Administration of oral oxytetracycline in milk replacer will result in lower bioavailability. {R-111}

**USP requirements:** Preserve in well-closed containers. A mixture of Oxytetracycline Hydrochloride and one or more suitable excipients. Label it to indicate that it is for oral veterinary use only. Contains the labeled amount, within ±10%. Meets the requirements for Identification, pH (1.5–3.0, in the solution obtained as directed in the labeling), Loss on drying (not more than 3.0%, and Minimum fill. {R-128}

## OXYTETRACYCLINE FOR MEDICATED FEED

### Usual dose:

*Bees, honey*—Foul brood: Oral, 200 mg per colony of bees every four to five days in the spring and/or fall {**R-117**}. Powder is dusted on the outer parts of the frames or mixed as a syrup and fed in feeder pails or in the combs {**R-117**}.

Note: Honey from infected colonies should not be used for the preparation of medicated syrup {**R-117**}.

### *Calves*—

Bacterial enteritis: Oral, 22 mg per kg of body weight a day {**R-117**}.

Note: Canadian labeling lists a dose of 50 grams per ton (55 grams per metric ton [1000 kg]) in the treatment of bacterial enteritis {**R-26**}.

Improved feed efficiency<sup>1</sup>; or increased weight gain<sup>1</sup> in calves weighing less than 113.6 kg (250 pounds): Oral 0.11 to 0.22 mg per kg of body weight a day, administered in the feed and fed as the only ration {**R-117**}.

Improved feed efficiency<sup>1</sup>; or increased weight gain<sup>1</sup> in calves weighing 113 to 181 kg (250 to 400 pounds): Oral, 25 mg per animal a day, administered in the feed and fed as the only ration {**R-117**}.

Note: According to product labeling, when administered in milk replacer, the 22 mg per kg of body weight dose is indicated in the treatment of bacterial enteritis only {**R-117**}.

*Catfish*<sup>1</sup>—Hemorrhagic septicemia; or pseudomonas disease: Oral 55 to 82.5 mg per kg of body weight a day for a maximum of ten days, administered in the feed and fed as the only ration {**R-27**}.

### *Cattle*—

Bacterial enteritis<sup>1</sup>: Oral, 22 mg per kg of body weight a day {**R-117**}.

Bacterial pneumonia, acute (prophylaxis and treatment)<sup>1</sup>: Oral, 500 to 2000 mg (2 grams) per animal a day, administered in the feed and fed as the only ration for three to five days prior to shipping and three to five days after shipping {**R-122; 117**}.

Bacterial pneumonia (treatment)<sup>1</sup>: Oral, 22 mg per kg of body weight a day, administered in feed and fed as the only ration for seven to fourteen days {**R-117**}.

Improved feed efficiency<sup>1</sup>; or increased weight gain<sup>1</sup>, in growing cattle weighing over 400 pounds: Oral, 75 mg per animal a day, administered in the feed and fed as the only ration {**R-117**}.

[Bloat]—Oral, 75 mg per animal a day, administered in the feed and fed as the only ration {**R-26**}.

### *Chickens*—

Chronic respiratory disease, specifically air sacculitis, reduction in associated mortality<sup>1</sup>: Oral, 500 grams per ton of feed, fed as the only ration {**R-117**}.

Chronic respiratory disease (control): Oral, 400 grams per ton of feed, fed as the only ration {**R-117**}.

Note: Canadian labeling lists a dose of 100 grams per ton (110 grams per metric ton [1000 kg]) in the treatment of chronic respiratory disease {**R-26**}.

Fowl cholera<sup>1</sup>; or synovitis: Oral, 100 to 200 grams per ton of feed, fed as the only ration {**R-117**}.

Improved feed efficiency<sup>1</sup> and increased weight gain<sup>1</sup>: Oral, 10 to 50 grams per ton of feed, fed as the only ration {**R-117**}.

*Lobsters*—Gaffkemia: Oral, 2.2 grams per kg of feed, fed as the only ration {**R-27; 124**}.

### *Pigs*—

Bacterial enteritis: Oral, 22 mg per kg of body weight a day, administered in the feed and fed as the only ration {**R-117**}.

Note: Canadian labeling lists a dose of 100 grams per ton (110 grams per metric ton [1000 kg]) in the treatment of bacterial enteritis {**R-26**}.

For reducing the shedding of leptospirosis and reducing the incidence of associated abortions: Oral, 22 mg per kg of body weight per animal a day, administered in the feed and fed as

the only ration **{R-117}**.

Note: Canadian labeling lists a dose of 500 grams per ton (550 grams per metric ton [1000 kg]) in the treatment of leptospirosis **{R-26}**.

Improved feed efficiency and increased weight gain<sup>1</sup>: Oral, 10 to 50 grams per ton of feed, fed as the only ration **{R-117}**.

[Atrophic rhinitis]: Oral, 50 grams per ton (55 grams per metric ton [1000 kg]) of feed, fed as the only ration **{R-26}**.

Note: Different feeding regimens will result in differences in actual mg of oxytetracycline per kg of body weight consumed by individual pigs **{R-110}**.

Therapeutic serum concentrations of > 0.5 mcg/mL were not produced when 550 mg of oxytetracycline per kg of feed was administered to 30-kg pigs in one study **{R-107}**.

An oral dose of 54 to 108 mg per kg of body weight a day (concentrations of 1600 and 2400 mg of oxytetracycline per kg of feed) was reported to be required to produce 1 mcg per mL serum concentrations in pigs **{R-110}**.

*Salmon, Pacific*<sup>1</sup>—Marking of skeletal tissue: Oral, 250 mg per kg of body weight a day **{R-27}**.

*Salmonids*—[Cold water disease]; [columnaris disease]; [enteric red-mouth disease]; furunculosis; hemorrhagic septicemia<sup>1</sup>; pseudomonas disease<sup>1</sup>; or ulcer disease: Oral, 55 to 82.5 mg per kg of body weight a day, administered in the feed and fed as the only ration **{R-27; 124}**.

*Sheep*<sup>1</sup>—

Bacterial enteritis; or bacterial pneumonia: Oral 22 mg per kg of body weight per animal a day, administered in the feed and fed as the only ration **{R-117}**.

Improved feed efficacy and increased weight gain: Oral, 10 to 20 grams per ton of feed, fed as the only ration **{R-117}**.

*Turkeys*—

Bacterial enteritis (bluecomb): Oral, 55 mg per kg of body weight a day, administered in the feed and fed as the only ration **{R-117}**.

Note: Canadian labeling lists a dose of 100 grams per ton (110 grams per metric ton [1000 kg]) of feed, fed as the only ration **{R-26}**.

Hexamitiasis<sup>1</sup>: Oral, 100 grams per ton of feed, fed as the only ration **{R-117}**.

Improved feed efficiency<sup>1</sup> and increased weight gain<sup>1</sup>: Oral, 10 to 50 grams per ton of feed, fed as the only ration **{R-117}**.

Synovitis: Oral, 200 grams per ton of feed, fed as the only ration **{R-26}**.

[Sinusitis]: Oral, 100 grams per ton (110 grams per metric ton [1000 kg]) of feed, fed as the only ration **{R-26}**.

[*Lambs*]—

Bacterial enteritis: Oral, 100 grams per ton (110 grams per metric ton [1000 kg]) of feed, fed as the only ration **{R-26}**.

Enterotoxemia: Oral, 20 grams per ton (22 grams per metric ton [1000 kg]) of feed, fed as the only ration **{R-26}**.

Note: Environmental and health conditions may affect the intake of water and the amount of medication consumed. **{R-17}** Administration of medication by food or water to animals with pneumonia or other infections can be affected by reduced feed and water intake **{R-09}**.

#### **Strength(s) usually available {R-58}:**

U.S.— **{R-62; 122}**

Veterinary-labeled products:

110 grams per kg of premix (OTC) [*OTC 50; OXTC 50; Pennox 50 Meal; Terramycin 50*].

220 grams per kg of premix (OTC) [*OXTC 100; Pennox 100 Hi-Flo Meal; Pennox 100-MR; Terramycin 100; Terramycin 100 For Fish*].

440 grams per kg of premix (OTC) [*OXTC 200; Pennox 200 Hi-Flo Meal; Terramycin 200*].

Canada— **{R-26; 55}**

Veterinary-labeled products:

110 grams per kg of premix (OTC) [*Oxy-110; Oxysof-110; Oxytetracycline 50; Terramycin-50*].

220 grams per kg of premix (OTC) [*Oxy-220; OxySol-220; Oxytetracycline 100; Terramycin -100*].

440 grams per kg of premix (OTC) [*Oxy-440; OxySol-440; Oxytetracycline 200; Terramycin -200; Terramycin-Aqua*].

**Withdrawal times {R-58}:**

Note: *Bees*—To avoid contamination of honey, oxytetracycline hydrochloride soluble powder should be fed early in the spring or fall before the main honey flow begins. Honey stored during therapy should be removed following the last medication and should not be used for human food {R-117}.

U.S.— {R-27; 186}

When fed 500 grams per ton of feed:

Species	Withdrawal time
	Meat (days)
<i>Chickens</i>	1
If fed low-calcium feed	3

Note: Not labeled for chickens producing eggs for human consumption {R-117}.

When fed up to 400 grams per ton of feed:

Species	Withdrawal time
	Meat (days)
<i>Chickens</i>	0
If fed low-calcium feed	3

Note: Not labeled for chickens producing eggs for human consumption {R-117}.

When fed up to 200 grams per ton of feed:

Species	Withdrawal time
	Meat (days)
<i>Turkeys</i>	0

Note: Not labeled for turkeys producing eggs for human consumption {R-117}.

When fed to turkeys at 200 grams or more per ton of feed, and to cattle, pigs, and sheep at 22 mg/kg:

Species	Withdrawal time
	Meat (days)
<i>Bees</i>	42 (honey)
<i>Catfish</i>	21
<i>Calves (some products), cattle, sheep, turkeys</i>	5
<i>Lobsters</i>	30
<i>Pacific salmon</i>	7
<i>Pigs</i>	0 or 5, depending on product
<i>Salmonids</i>	21

Note: Not labeled for poultry producing eggs for human consumption {R-117}. A withdrawal time has not been established for preruminating calves for some products {R-117}.

Canada {R-26; 55}—

Note: *Bees*—Withdraw medication 4 weeks prior to honey flow.

Species	Withdrawal time
	Meat (days)
<i>Bees</i>	28 (honey)
<i>Calves, cattle</i>	5
<i>Chickens, pigs, turkeys</i>	7
<i>Lambs</i>	4

<i>Lobsters</i>	30
<i>Salmonids</i> , 10 °C or warmer	40
<i>Salmonids</i> , below 10 °C	80

Note: Not labeled for chickens producing eggs for human consumption **{R-117}**. Withdrawal time has not been established for preruminating calves **{R-117}**.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

**Preparation of dosage form:** For use in dry feeds only, as indicated on manufacturer's labeling. Should not be used without diluting. **{R-122}**

**Incompatibilities:** Salmonid and lobster feeds having a high ash content (calcium, copper, iron, or zinc) may bind oxytetracycline and prevent absorption. Oxytetracycline also should not be administered with feeds containing bentonite. **{R-124}**

**Additional information:** U.S.—For fish, this medication should not be used when water temperature is below 16.7 °C (62 °F) for catfish or below 9 °C (48.2 °F) for salmonids. **{R-62}**

**USP requirements:** Not in USP.

## OXYTETRACYCLINE TABLETS USP

### Usual dose:

Bacterial enteritis<sup>1</sup>; or

Bacterial pneumonia<sup>1</sup>—*Calves*:

Control—Oral, 5.5 mg per kg of body weight every twelve hours.

**{R-2; 60}**

Treatment—Oral, 11 mg per kg of body weight every twelve hours for up to four days. **{R-2; 60}**

### Strength(s) usually available **{R-58}**:

U.S.— **{R-2; 60}**

Veterinary-labeled products:

250 mg (OTC) [*Terramycin Scours Tablets*].

500 mg (OTC) [*Oxy 500 Calf Bolus*].

1000 mg (OTC) [*Oxy 1000 Calf Bolus*].

Canada—

Veterinary-labeled products:

Not commercially available.

### Withdrawal times:

U.S.— **{R-60}**

Species	Withdrawal time
	Meat (days)
<i>Calves</i>	0 or 7, depending on product

Note: Product labeling with the above withdrawal time states that it applies when calves are treated for up to four days.

Products are not labeled for use in preruminating calves **{R-58}**.

**USP requirements:** Preserve in tight, light-resistant containers. Contain the labeled amount, within -10% to +20%. Meet the requirements for Identification, Dissolution (75% in 45 minutes in 0.1 N hydrochloric acid in Apparatus 1 at 100 rpm), Uniformity of dosage units, and Water (not more than 7.5%). **{R-128}**

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

## OXYTETRACYCLINE INJECTION USP

### Usual dose:

*Cattle*—Actinobacillosis<sup>1</sup>; anaplasmosis<sup>1</sup>; [bacterial arthritis]; bacterial enteritis; [blackleg/malignant edema]; diphtheria<sup>1</sup>; [leptospirosis]; [mastitis]; [omphalophlebitis]; [peritonitis]; pneumonia and bovine respiratory disease complex; pododermatitis; skin and soft tissue infections<sup>1</sup>; or uterine infections: Intramuscular or intravenous, 6.6 to 11 mg per kg of body weight every twenty-four hours. **{R-10; 24; 25; 121}**

Note: For *uterine infections* in cattle, an [intravenous dose of 11 mg per kg of body weight every eight to twelve hours]<sup>1</sup> has been recommended, based on distribution studies **{R-104}**. The shortened dosing interval will require an extended withdrawal time **{R-14}**.

For *pneumonia* caused by *Pasteurella*, an [intravenous dose of 11 mg per kg of body weight every twelve hours]<sup>1</sup> has been recommended, based on pharmacokinetic changes in calves with induced pneumonia **{R-106}**; however, this regimen is usually reserved for serious cases. The shortened dosing interval will require an extended withdrawal time **{R-14}**.

For [*thromboembolic meningoencephalitis*]<sup>1</sup>, a dose of 11 mg per kg of body weight every twenty-four hours has been recommended; however, there are no specific research data to support the efficacy of this use **{R-178; 179}**.

[*Pigs*]<sup>1</sup>—Bacterial enteritis; bacterial pneumonia; erysipelas; leptospirosis; mastitis; or uterine infections: Intramuscular or intravenous, 6.6 to 11 mg per kg of body weight every twenty-four hours. **{R-10}**

Note: No more than 10 mL should be injected per site in adult cattle and no more than 5 mL per site in pigs. Less mature animals should have decreasing volumes injected per site (but not total mg per kg of body weight) so that small animals receive 0.5 to 2 mL per injection site. Intravenously administered oxytetracycline should be injected slowly. **{R-21}**  
Intramuscularly administered oxytetracycline causes a notable tissue reaction (see note on slaughter trim below under *Withdrawal times*).

[*Horses*]<sup>1</sup>—Ehrlichiosis (*Ehrlichiosis equi*); or Potomac horse fever (*Ehrlichiosis risticii*): Intravenous, 10 mg per kg of body weight every twenty-four hours. **{R-46-48; 92; 138}**

Note: Gastrointestinal side effects are possible following oxytetracycline administration to horses.

The above dose is based on clinical trials and retrospective dose-response studies.

[*Foals*]<sup>1</sup>—Although the efficacy and safety have not been established, a single intravenous dose of 44 mg of oxytetracycline per kg of body weight has been used in the treatment of *flexural limb deformities* in newborn foals, based on controlled studies in healthy foals **{R-157; 158}**. The dose is most often administered as a single intravenous dose of 2 to 3 grams per foal **{R-158}** or as an intravenous dose of 1.5 grams per foal, repeated in twenty-four hours. In some cases, clinicians have repeated an initial 2- to 3-gram dose twenty-four hours following the initial dose **{R-20; 157}**.

Studies have demonstrated the safety, including lack of renal toxicity, of doses of up to 54.5 to 75 mg per kg of body weight, administered two times, twenty-four hours apart, to twenty newborn foals **{R-20; 158}**; however, because high doses of oxytetracyclines have been associated with renal toxicity in many species **{R-15}**, some clinicians prefer to test renal function before treatment. It is recommended that this high dose of oxytetracycline not be administered to foals with any systemic illness or disorder

predisposing to renal compromise, including dehydration or endotoxemia.

[*Sheep*]—Bacterial arthritis; bacterial pneumonia; mastitis; or uterine infections: Intramuscular or intravenous, 6.6 mg per kg of body weight every twenty-four hours **{R-24; 121}**.

**Strength(s) usually available {R-58}:**

U.S.—

Veterinary-labeled products:

100 mg per mL (OTC) [*Agrimycin 100; AmTech Maxim -100; Duramycin 100; Oxybiotic -100; Oxy cure 100; Oxy-Mycin 100; Promycin 100; Terra -Vet 100; Tetroxy-100*].

Canada—

Veterinary-labeled products:

100 mg per mL (OTC) [*Oxy LP; Oxymycine LP; Oxytetracycline 100LP; Oxytetramycin 100; Oxyvet 100 LP; Tetraject LP*].

**Withdrawal times {R-58}:**

U.S.— **{R-21; 56}**

Species	Withdrawal time	
	Meat (days)	
<i>Cattle</i>	18, 19, 20, or 22, depending on product	
<i>Pigs</i>	26	

Note: Product labeling listing the above withdrawal times states that they apply to a dose of 6.6 to 11 mg per kg of body weight a day in cattle and pigs for a maximum of four days. Not labeled for use in lactating cattle or preruminating calves.

Cattle slaughtered within 20 days of intramuscular administration of oxytetracycline may require trimming of the injection sites and surrounding tissues during dressing procedure.

Canada— **{R-24}**

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cattle</i>	18	60 or 72, depending on product
<i>Pigs, sheep</i>	18	

Note: The above withdrawal times are based on Canadian labeling that lists a dose of 6.6 mg per kg of body weight a day for a maximum of two to three days. **{R-24}**

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

**Preparation of dosage form:** For intravenous administration, dilution in water for injection or physiological saline is recommended. Doses of up to 2500 mg (50 mL) can be diluted in 250 mL of diluent, and larger doses in 500 mL of diluent.

**Stability:** Diluted medication should be used or discarded immediately after mixing. **{R-21}** Solution may darken on standing but this color change does not affect the potency of the medication.

**USP requirements:** Preserve in single-dose or in multiple-dose containers, protected from light. A sterile solution of Oxytetracycline with or without one or more suitable anesthetics, antioxidants, buffers, complexing agents, preservatives, and solvents. Contains the labeled amount, within -10% to +20%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, and pH (8.0-9.0). **{R-128}**

## OXYTETRACYCLINE INJECTION USP (LONG-ACTING)

Note: The formulations listed below have a viscosity excipient intended to prolong therapeutic serum antibiotic concentrations. These products are believed to differ from other oxytetracycline injection products only in the rate of absorption from intramuscular injection; moreover, some studies using oxytetracycline products with 2-pyrrolidone viscosity excipient have failed to show that the duration of action is significantly prolonged over that of the conventional formulation after intramuscular injection, when they are administered at the same dose. **{R-107; 162}**. As such, use of the long-acting formulations at standard doses of 6 to 11 mg per kg of body weight may not result in a prolonged duration of action. Also, there is no difference in duration of action between conventional and long-acting formulations when they are administered intravenously **{R-99; 151}**.

### Usual dose:

**Cattle**—Actinobacillosis<sup>1</sup>; bacterial enteritis<sup>1</sup>; bacterial pneumonia and bovine respiratory disease complex; diphtheria<sup>1</sup>; keratoconjunctivitis; leptospirosis; metritis, acute<sup>1</sup>; pododermatitis; or skin and soft tissue infections<sup>1</sup>: Intramuscular, intravenous, or, when labeled, subcutaneous, 6.6 to 11 mg per kg of body weight every twenty-four hours for four days **{R-3; 45}**.

Note: When it is impractical to give cattle more than a single dose for the treatment of keratoconjunctivitis or pneumonia, an intramuscular or, when labeled, subcutaneous dose of 20 mg per kg of body weight administered as a single dose is recommended. **{R-45}**

In calves, [40 mg per kg of body weight as a single dose]<sup>1</sup> has been used in the treatment of *bacterial pneumonia* that is unresponsive to 20 mg per kg of body weight, based on pharmacokinetic and toxicity data **{R-95; 101}**; however, the clinical efficacy was not established in this study. This higher dose should not be repeated because of the risk of adverse effects **{R-30; 167; 168}**.

For [*thromboembolic meningoencephalitis*]<sup>1</sup> in cattle, a dose of 11 mg per kg of body weight every twenty-four hours has been recommended; however, there are no specific research data to support the efficacy of this use **{R-178; 179}**.

**Pigs**—Bacterial enteritis<sup>1</sup>; bacterial pneumonia; or leptospirosis:

Intramuscular, 6.6 to 11 mg per kg of body weight every twenty-four hours for four days. **{R-45}**

Note: When it is impractical to give pigs more than a single dose for the treatment of pneumonia, an intramuscular dose of 20 mg per kg of body weight administered as a single dose is recommended. **{R-45}**

**Sows**—Bacterial enteritis in suckling pigs: Intramuscular, 6.6 mg per kg of body weight, administered once eight hours before farrowing or immediately after farrowing. **{R-45}**

Note: No more than 10 mL should be administered intramuscularly at any one site in adult cattle. No more than 5 mL should be injected intramuscularly at any one site in adult pigs. **{R-45}** Injections should be administered deep into the fleshy part of the muscle. **{R-25}** Less mature animals should have size-dependent decreasing volumes injected per site so that small calves receive only 1 to 2 mL per injection site.

### Strength(s) usually available **{R-58}**:

U.S.— **{R-3; 45}**

Veterinary-labeled products:

200 mg per mL (OTC) [*Agrimycin 200; AmTech Maxim -200; Biomylin 200; Duramycin 72-200; Geomylin 200; Liquamycin LA-200; Maxim-200; OT 200; OxyBiotic-200; Oxy cure 200; Oxy-Mycin 200; Oxyshot LA; Pennox 200 Injectable*].

Note: The above products contain the following viscosity excipients: *Biomylin 200* contains polyethylene glycol; *Duramycin 72-200, Liquamycin LA-200, Maxim-200*; and *Pennox 200* contain 2-pyrrolidone; and *Oxyshot LA* contains *N*-methylpyrrolidone.

Canada— {R-25; 120}

Veterinary-labeled products:

200 mg per mL (OTC) [*Alamycin LA*; *Biomycin 200*; *Liquamycin LA-200*; *Oxy LA*; *Oxymycine LA*; *Oxyvet 200 LA*; *Tetraject LA*].

300 mg per mL (OTC) [*Tetradure LA 300*].

**Withdrawal times {R-58}:**

U.S.— {R-3; 5; 45; 153}

Note: If oxytetracycline injection is administered to calves as a single intramuscular dose of 40 mg per kg of body weight, there is some evidence to suggest that a withdrawal time of 49 days would be sufficient to avoid residues, based on tissue depletion studies of the parent drug {R-101}.

Species	Withdrawal time	
	Meat (days)	
<i>Cattle</i>	28	
<i>Pigs</i>	28 or 42, depending on product	

Note: Some products are not labeled for use in lactating dairy cattle and list the above withdrawal times. Product labeling listing the above withdrawal times states that they apply to a dose of 6.6 to 11 mg per kg of body weight a day for a maximum of four days or 20 mg per kg of body weight administered as a single dose.

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cattle</i>	28	96
<i>Pigs</i>	28	

Note: Product labeling listing the above withdrawal times states that they apply to a dose of 6.6 to 11 mg per kg of body weight a day for a maximum of four days or 20 mg per kg of body weight administered as a single dose.

Canada— {R-25; 120}

Species	Withdrawal time	
	Meat (days)	
<i>Cattle and pigs</i> Intramuscular injection	21 or 28, depending on product	
<i>Cattle</i> Subcutaneous injection	48	

Note: Product labeling listing the above withdrawal times states that they apply to a dose of 20 mg per kg of body weight administered once. Not labeled for use in lactating dairy cattle. One product recommends a 42-day withdrawal to avoid excess trim at the injection site {R-58}.

**Packaging and storage:** Store between 15 and 30° C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing. {R-45}

**Preparation of dosage form:** Warm to room temperature before administration.

**USP requirements:** Preserve in single-dose or in multiple-dose containers, protected from light. A sterile solution of Oxytetracycline with or without one or more suitable anesthetics, antioxidants, buffers, complexing agents, preservatives, and solvents. Contains the labeled amount, within -10% to +20%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, and pH (8.0-9.0). {R-128}

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

## TETRACYCLINE

### Additional Dosing Information

When possible, oral tetracycline should be administered 1 hour before or 2 hours after milk replacer. **{R-1}**

### Mucosal Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### TETRACYCLINE UTERINE TABLETS

#### Usual dose:

Note: [*Cows*] and [*mares*].—Although the efficacy and safety are not currently established, the use of a 4-gram bolus administered as a single intrauterine dose is included in Canadian product labeling **{R-9}** for the treatment of *uterine infections*. The dose may be repeated in two days if necessary. **{R-9}**

#### Strength(s) usually available:

U.S.—

Veterinary-labeled products:  
Not commercially available.

Canada—**{R-9}**

Veterinary-labeled products:  
4 grams (OTC) [*Tetra 4000; Tetrabo*].

#### Withdrawal times:

Canada—**{R-9}**

Species	Withdrawal time	
	Meat (days)	Milk (hours)
<i>Cows</i>	18	72

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer.

**Auxiliary labeling:** • Protect from excessive moisture. **{R-9}**

**USP requirements:** Not in USP.

### Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

### TETRACYCLINE BOLUSES USP

**Usual dose:** Bacterial enteritis; or bacterial pneumonia—*Calves*: Oral, 11 mg per kg of body weight every twelve hours for five days. **{R-1}**

#### Strength(s) usually available **{R-58}**:

U.S.—**{R-1}**

Veterinary-labeled products:  
500 mg (OTC) [*Calf Scour Bolus Antibiotic; 5-Way Calf Scour Bolus*].

Canada—**{R-9}**

Veterinary-labeled products:  
4 grams (OTC) [*Tetra 4000; Tetrabo*].

**Withdrawal times **{R-58}**:**

U.S.— {R-1}	
Species	Withdrawal time
	Meat (days)
<i>Calves</i>	12, 14 or 24, depending on product

Canada— {R-9}	
Species	Withdrawal time
	Meat (days)
<i>Calves</i>	5
<i>Cattle</i>	18

Note: Product labeling with the above withdrawal times state that they apply to a dose of 20 mg per kg of body weight a day for three to five days.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

**Auxiliary labeling:** • Protect from excessive moisture. {R-9}

**USP requirements:** Preserve in tight containers. Label Boluses to indicate that they are intended for veterinary use only. Contain the equivalent of the labeled amount of tetracycline hydrochloride, within –10% to +20%. Meet the requirements for Identification, Uniformity of dosage units, and Loss on drying (not more than 3.0%; or for Boluses greater than 15 mm in diameter, not more than 6.0%). {R-128}

#### TETRACYCLINE HYDROCHLORIDE CAPSULES USP

**Usual dose:** [Rocky Mountain spotted fever]<sup>1</sup>—*Dogs:* Oral, 22 mg per kg of body weight every eight hours for fourteen days. {R-140; 141}

Note: [*Dogs*]<sup>1</sup>—The above dose is based on clinical trials and retrospective dose-response studies. The same dosage regimen has also been used in the treatment of *ehrlichiosis* in dogs {R-43; 139}, although the efficacy of this treatment has not been confirmed.

A dose of 22 mg per kg of body weight every six to eight hours has also been used in the treatment of other susceptible *bacterial infections* in dogs.

Dosing trials suggest that 30 mg of oral tetracycline per kg of body weight every twelve hours for twenty-eight days, administered in conjunction with 20 mg of intramuscular streptomycin every twenty-four hours for the first fourteen days, may be successful in resolving *brucellosis* in dogs. It has been recommended that all dogs be treated in a population in which some have tested positive for brucellosis; good management practices are recommended and repeated follow-up testing is needed for several months to confirm that all dogs remain seronegative {R-160}.

See also *Tetracycline Oral Suspension USP*.

#### Strength(s) usually available:

U.S.—

Veterinary-labeled products:  
Not commercially available.

Human-labeled products:  
250 mg (Rx) [*Achromycin V*; GENERIC].  
500 mg (Rx) [*Achromycin V*; GENERIC].

Canada—

Veterinary-labeled products:  
Not commercially available.

Human-labeled products:  
250 mg (Rx) [*Apo-Tetra*; *Novo-Tetra*; *Nu-Tetra*].

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

**USP requirements:** Preserve in tight, light-resistant containers. Contain the labeled amount, within -10% to +25%. Meet the requirements for Identification, Dissolution (80% in 60 minutes, 90 minutes for 500-mg capsules, in water in Apparatus 2 at 75 rpm), Uniformity of dosage units, Loss on drying (not more than 4.0%), and Limit of 4-epianhydrotetracycline (not more than 3.0%). **{R-128}**

**TETRACYCLINE HYDROCHLORIDE SOLUBLE POWDER USP**

**Usual dose:**

*Calves and pigs*—Bacterial enteritis; or bacterial pneumonia: Oral, 11 mg per kg of body weight every twelve hours, administered in the only source of drinking water for three to five days. **{R-19}**

*Chickens*—Chronic respiratory disease; or infectious synovitis: Oral, 27.5 mg per kg of body weight every twelve hours, administered in the only source of drinking water for seven to fourteen days. **{R-19}**

*Turkeys*—Infectious synovitis; or bacterial enteritis: Oral, 27.5 mg per kg of body weight every twelve hours, administered in the only source of drinking water for seven to fourteen days. **{R-19}**

*[Sheep]*—Bacterial enteritis; or respiratory tract diseases: Oral, 40 mg per kg of body weight every twelve hours for four to five days **{R-18}**.

Note: Environmental and health conditions may affect the intake of water and the amount of medication consumed. **{R-17}** Administration of medication by food or water to animals with pneumonia or other infections can be affected by reduced feed and water intake **{R-109}**.

**Strength(s) usually available {R-58}:**

U.S.—**{R-8; 19}**

Veterinary-labeled products:

25 grams per pound of powder (OTC) [*Duramycin 10; PolyOtic Soluble Powder; Solu-Tet; Tet-Sol 10*].

324 grams per pound of powder (OTC) [*AmTech Tetracycline Hydrochloride Soluble Powder-324; Duramycin -324; Solu-Tet 324; Tet-324; Tetra Bac 324; Tetrasol Soluble Powder; Tet-Sol 324; GENERIC*].

Canada—**{R-18}**

Veterinary-labeled products:

55 mg per gram of powder (OTC) [*Tetra 55; GENERIC*].

62.5 mg per gram of powder (OTC) [*Onycin 62.5; Tetracycline 62.5 Soluble Powder*].

250 mg per gram of powder (OTC) [*Onycin 250; Tetra 250; Tetracycline 250; Tetracycline 250 Concentrate Soluble Powder; Tetramed 250*].

1000 mg per gram of powder (OTC) [*Onycin 1000; Tetra 1000; Tetracycline 1000; Tetramed 1000*].

**Withdrawal times:**

U.S.— **{R-8; 19}**

Species	Withdrawal time
	Meat (days)
<i>Calves</i>	4 or 5, depending on product
<i>Chickens, pigs, turkeys</i>	4 or 7, depending on product

Note: Products are not labeled for use in preruminating calves or poultry producing eggs for human consumption **{R-58}**.

Canada— **{R-18}**

Species	Withdrawal time
	Meat (days)
<i>Calves, chickens, pigs, sheep, turkeys</i>	5

Note: Product labeling with the above withdrawal time states that it applies to a dose of 20 to 40 mg per kg of body weight every twelve hours for a maximum of five days for calves, pigs, and sheep and a dose of 200 mg per liter of water for three to five days for chickens and turkeys. Although a milk withdrawal time is included on one product label, these products are not specifically labeled for use in lactating dairy cows in Canada. Products are not labeled for use in laying hens **{R-18; 58}**.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer.

**Preparation of dosage form:** Fresh solutions should be prepared every 24 hours when administered in plastic or stainless steel waterers and every 12 hours when administered in galvanized waterers.

**Stability:** Solutions are stable for 24 hours. **{R-8}**

**USP requirements:** Preserve in tight containers. Label it to indicate that it is intended for veterinary use only. Contains the labeled amount, within –10% to +25%. Meets the requirements for Identification and Loss on drying (not more than 2.0%). **{R-128}**

### TETRACYCLINE ORAL SUSPENSION USP

**Usual dose:** Bacterial gastroenteritis<sup>1</sup>; or urinary tract infections<sup>1</sup>—*Cats* and *dogs*: Oral, 14 to 22 mg per kg of body weight every six to eight hours. **{R-177}**

See also *Tetracycline Hydrochloride Capsules USP*.

#### Strength(s) usually available:

U.S.— **{R-4}**

Veterinary-labeled products:

100 mg per mL (Rx) [*Panmycin Aquadrops*].

Canada— **{R-126}**

Veterinary-labeled products:

Not commercially available.

**Packaging and storage:** Store between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer. Protect from light.

**Auxiliary labeling:** • Shake well before each dose **{R-4}**.

**USP requirements:** Preserve in tight, light-resistant containers. It is Tetracycline with or without one or more suitable buffers, preservatives, stabilizers, and suspending agents. Contains the equivalent of the labeled amount of tetracycline hydrochloride, within –10% to +25%. Meets the requirements for Identification, Uniformity of dosage units (single-unit containers), Deliverable volume, pH (3.5–6.0), and Limit of 4-epianhydrotetracycline (not more than 5.0%). **{R-128}**

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<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

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Developed: 07/17/96

Revised: 7/14/98; 10/12/99; 6/30/02; 04/05/03

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