

MAR 16 1999

Date of Approval:

## FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

**ANADA 200-008**

**OXY-TET™ 200; BIO-MYCIN® 200**

**(oxytetracycline injection)**

“...for establishment of a 28-day withdrawal period for subcutaneous use in cattle and intramuscular use in swine, thereby establishing a 28-day withdrawal period for all approved routes of administration in cattle and swine.”

Sponsored by:

Boehringer Ingelheim Vetmedica, Inc.

ANADA 200-008

FOIS 1

I. GENERAL INFORMATION .....1

II. INDICATIONS FOR USE .....1

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE .....2

    A. Dosage Form .....2

    B. Route(s) of Administration and Recommended Dosage.....2

IV. EFFECTIVENESS.....4

V. ANIMAL SAFETY .....4

VI. HUMAN SAFETY .....5

VII. AGENCY CONCLUSIONS .....9

VIII. APPROVED LABELING .....9

## I. GENERAL INFORMATION

ANADA Number:	200-008
Sponsor:	Boehringer Ingelheim Vetmedica, Inc. 2621 North Belt Highway St. Joseph, Missouri 64506
Established Name:	oxytetracycline injection
Proprietary Names:	OXY-TET™ 200 BIO-MYCIN® 200*
Marketing Status:	OTC
Supplemental Effect:	Establishes a 28-day withdrawal period for subcutaneous use of this product in cattle and intramuscular use of this product in swine, thereby establishing a 28-day withdrawal period for all approved routes of administration in cattle and swine.
References:	Freedom of Information Summaries dated November 16, 1994, for the original approval, and May 22, 1996, for the supplemental approval for subcutaneous use in cattle.

\*OXY-TET™ 200 will hereafter denote both OXY-TET™ 200 and BIO-MYCIN® 200.

## II. INDICATIONS FOR USE

OXY-TET™ 200 is intended for use in the treatment of the following diseases in beef cattle, nonlactating dairy cattle, and swine when due to oxytetracycline susceptible organisms:

### BEEF CATTLE AND NONLACTATING DAIRY CATTLE

OXY-TET™ 200 is indicated in the treatment of pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Haemophilus* spp.; infectious bovine keratoconjunctivitis (pinkeye) caused by *Moraxella bovis*; foot rot and diphtheria caused by *Fusobacterium necrophorum*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; leptospirosis caused by *Leptospira pomona*; and wound infections and acute metritis caused by strains of staphylococci and streptococci organisms sensitive to oxytetracycline.

## SWINE

In swine, OXY-TET™ 200 is indicated in the treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*; pneumonia caused by *Pasteurella multocida*; and leptospirosis caused by *Leptospira pomona*.

In sows, OXY-TET™ 200 is indicated as an aid in the control of infectious enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

### III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE

#### A. Dosage Form

OXY-TET™ 200 is a sterile injectable solution available in 100-, 250-, and 500-mL bottles. Each milliliter contains 200 mg oxytetracycline.

#### B. Route(s) of Administration and Recommended Dosage

##### BEEF CATTLE AND NONLACTATING DAIRY CATTLE

OXY-TET™ 200 is to be administered by intramuscular, subcutaneous, or intravenous injection to beef cattle and nonlactating dairy cattle.

A single dose of 9 mg of OXY-TET™ 200 per pound of body weight administered intramuscularly or subcutaneously is recommended in the treatment of the following conditions: 1) bacterial pneumonia caused by *Pasteurella* spp. (shipping fever) in calves and yearlings, where retreatment is impractical due to husbandry conditions, such as cattle on range, or where repeated restraint is inadvisable; 2) infectious bovine keratoconjunctivitis (pinkeye) caused by *Moraxella bovis*.

OXY-TET™ 200 can also be administered by intravenous, intramuscular, or subcutaneous injection at a level of 3 to 5 mg of oxytetracycline per pound of body weight per day. In the treatment of severe foot rot and advanced cases of other indicated diseases, a dosage level of 5 mg per pound of body weight per day is recommended. Treatment should be continued 24 to 48 hours following remission of disease signs; however, treatment is not to exceed a total of four consecutive days. Consult your veterinarian if improvement is not noted within 24 to 48 hours of the beginning of treatment.

No more than 10 mL should be injected intramuscularly or subcutaneously at any one site in adult beef cattle and nonlactating dairy cattle; rotate injection sites for each succeeding treatment. The volume administered per injection site should be adjusted according to age and body size so that 1 to 2 mL per injection site is injected in small calves.

## SWINE

A single dose of 9 mg of OXY-TET™ 200 per pound of body weight administered intramuscularly is recommended in the treatment of bacterial pneumonia caused by *Pasteurella multocida* in swine, where retreatment is impractical due to husbandry conditions or where repeated restraint is inadvisable.

OXY-TET™ 200 can be administered by intramuscular injection at a level of 3 to 5 mg of oxytetracycline per pound of body weight per day. Treatment should be continued 24 to 48 hours following remission of disease signs; however, treatment is not to exceed a total of four consecutive days. Consult your veterinarian if improvement is not noted within 24 to 48 hours of the beginning of treatment.

For sows, administer once intramuscularly 3 mg of oxytetracycline per pound of body weight approximately 8 hours before farrowing or immediately after completion of farrowing.

For swine weighing 25 lb of body weight and under, OXY-TET™ 200 should be administered undiluted for treatment at 9 mg/lb but should be administered diluted for treatment at 3 or 5 mg/lb.

No more than 5 mL of OXY-TET™ 200 should be injected intramuscularly per site in adult swine; rotate injection sites for each succeeding treatment.

**IV. EFFECTIVENESS**

Since this supplemental application does not change the species, routes of administration, or dosages, no additional effectiveness studies were required. Studies conducted for the original ANADA approved November 16, 1994, and for the supplemental approval dated May 22, 1996, are summarized in the respective Freedom of Information Summaries.

**V. ANIMAL SAFETY**

The supplemental approval does not change the approved dose(s) of oxytetracycline, the frequency, or routes of administration. Accordingly, no additional studies were required for animal safety. See the Freedom of Information (FOI) Summaries for the approval of the original and supplemental applications of OXY-TET™ 200 approved November 16, 1994, and May 22, 1996, respectively.

## VI. HUMAN SAFETY

### A. Tolerances for residues

The FDA has established tolerances for the sum of residues of tetracyclines, including chlortetracycline, oxytetracycline, and tetracycline, in tissues of beef cattle, non-lactating dairy cows, calves, swine, sheep, chickens, turkeys, and ducks (61 FR 67453, December 23, 1996). The tolerances established for oxytetracycline under 21 CFR 556.500 are as follows: 2 ppm in muscle; 6 ppm in liver; and 12 ppm in kidney and fat.

### B. Residue depletion studies

#### 1. Subcutaneous administration in cattle

a. Study number: 635-0144-91B-004

b. Investigator: Bill C. Clymer, Ph.D.  
Clymer Research  
Amarillo, Texas

c. General design:

- (1) Purpose: This is a tissue residue depletion study for oxytetracycline injection, 200 mg/mL, conducted in beef calves. The study was conducted to comply with Good Laboratory Practices, 21CFR 58. Tissue analyses were conducted by Colorado Animal Research Enterprises (CARE), Fort Collins, Colorado 80524. The statistical analysis was conducted by Thomas J. Keefe, Ph.D., EnviroStat Associates, Fort Collins, Colorado 80526.
- (2) Animals: 20 healthy beef calves.
- (3) Dosage form: 200 mg/mL injectable solution
- (4) Route of administration: subcutaneous injection
- (5) Dose: a single treatment of 20 mg/kg, administered in the neck
- (6) Test duration: 11 days
- (7) Pertinent parameters measured: Approximately 500 g each of liver (cross-section of each lobe), 500 g each of injection site and noninjection site (semimembranosus) muscle, 200 g (or the maximum obtainable) abdominal fat, and both kidneys.

## d. Results

Residue analyses were conducted at CARE, using an adapted validated microbiological assay. The data are presented in Table 6.1.

Table 6.1: Oxytetracycline residues (Mean ± SD) in bovine tissues following a single subcutaneous administration of OXY-TET™ 200, at a dose of 20 mg/kg

Days*	Oxytetracycline (ppm)				
	Liver	Kidney	Muscle	Fat	Injection site
2	3.96±1.54	8.27±2.41	1.32±0.45	0.20±0.10	603.32±358.73
5	0.43±0.07	1.08±0.27	0.19±0.02	<LOQ	153.46±135.94
8	0.19±0.16	0.31±0.19	0.21	<LOQ	30.59±42.17
11	0.16±0.09	0.34±0.18	0.20	<LOQ	105.75±208.01

\*represents withdrawal time in days

LOQ = 0.1 ppm for kidney; 0.075 for liver, muscle, and fat

## 2. Intramuscular administration in swine

a. Study number: 635-0144-91B-021

b. Investigator: Diane Fagerberg, Ph.D.  
Colorado Animal Research Enterprises (CARE)  
Fort Collins, Colorado 80524

c. General design:

(1) Purpose: This is a tissue residue depletion study for oxytetracycline injection, 200 mg/mL, conducted in swine. The study was conducted to comply with Good Laboratory Practices, 21 CFR 58. Tissue analyses were conducted by CARE, Fort Collins, Colorado 80524. The statistical analysis was conducted by Thomas J. Keefe, Ph.D., EnviroStat Associates, Fort Collins, Colorado 80526.

(2) Animals: 24 healthy swine.

(3) Dosage form: 200 mg/mL injectable solution

(4) Route of administration: intramuscular injection

(5) Dose: a single treatment of 20 mg/kg, administered in the neck

(6) Test duration: 28 days

- (7) Pertinent parameters measured: Approximately 500 g each of liver (cross-section of each lobe), 500 g each of injection site and noninjection site (semimembranosus) muscle, 200 g (or the maximum obtainable) abdominal fat, and both kidneys.

d. Results

Residue analyses were conducted at CARE, using an adapted validated microbiological assay. The data are presented in Table 6.2.

Table 6.2: Oxytetracycline residues (Mean ± SD) in swine tissues following a single intramuscular administration of OXY-TET™ 200, at a dose of 20 mg/kg

Days*	Oxytetracycline (ppm)				
	Liver	Kidney	Muscle	Fat	Injection site
2	1.78±0.48	7.39±3.26	1.47±0.54	0.11±0.06	566.68±528.04
5	0.41±0.17	1.79±0.80	0.42±0.14	<LOQ	67.93±56.94
8	0.13±0.09	0.58±0.21	0.12±0.09	<LOQ	26.23±53.56
11	<LOQ	0.28±0.04	<LOQ	<LOQ	1.24
21	<LOQ	0.24±0.03	<LOQ	<LOQ	<LOQ
28	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

\*represents withdrawal time in days

LOQ = 0.1 ppm for kidney; liver, muscle, and fat

C. Withdrawal calculations

Withdrawal periods for the intramuscular, intravenous, and subcutaneous use of OXY-TET™ 200 in cattle, and for the intramuscular use of this drug in swine have previously been established in the original ANADA dated November 16, 1994, or in the supplemental application dated May 22, 1996. A withdrawal period of 28 days was assigned for the use of OXY-TET™ 200 in cattle *via* the intramuscular and intravenous routes of administration based on the blood level bioequivalence study conducted in support of the original ANADA. Because the study, conducted under CVM’s 1990 Bioequivalence Guidance, demonstrated blood level bioequivalence, a tissue residue depletion study was not required to support the approval. A withdrawal period of 42 days was assigned for the intramuscular use of OXY-TET™ 200 in swine based on a tissue residue depletion study conducted in support of the original ANADA approval. A withdrawal period of 36 days was assigned for the subcutaneous use of OXY-TET™ 200 in cattle based on a tissue residue study conducted in support of the supplemental ANADA dated May 22, 1996. See the FOI Summaries for ANADA 200008 dated November 16, 1994, and May 22, 1996, for additional information.

For this supplemental application, the withdrawal periods for the intramuscular use of OXY-TET™ 200 in swine and for the subcutaneous use of OXY-TET™ 200 in cattle have been recalculated. The recalculations were performed using the revised tetracycline tolerances (61 FR 67453), and a statistical tolerance limit algorithm for the 99<sup>th</sup> percentile with 95% confidence. As a result of these recalculations, a 28-day withdrawal period is assigned for the intramuscular administration of OXY-TET™ 200 in swine, and for the subcutaneous use of OXY-TET™ 200 in cattle. The 28-day withdrawal period for the intravenous and intramuscular administration of OXY-TET™ 200 in cattle, assigned as part of the original approval, remains unchanged.

D. Regulatory Analytical Method for Residues

The regulatory analytical method for detection of residues of the drug is a microbiological test using *Bacillus cereus* var. *mycoides* (ATCC 11778). The method is found in *Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports and Protocols*, Revised October 1968, Reprinted December 1974, National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204.

## VII. AGENCY CONCLUSIONS

The data submitted in support of this ANADA supplement satisfy the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. As a result of recalculations using the revised tetracycline tolerances (61 FR 67453), a 28-day withdrawal period is assigned for the intramuscular administration of OXY-TET™ 200 in swine, and for the subcutaneous use of OXY-TET™ 200 in cattle. The 28-day withdrawal period for the intravenous and intramuscular administration of OXY-TET™ 200 in cattle, assigned as part of the original approval, remains unchanged.

Adequate directions for use of the product to treat cattle and swine have been written for the layman, and the conditions for use prescribed on the labeling are likely to be followed in practice. Therefore, the Center for Veterinary Medicine (CVM) has concluded that this product shall continue to have over-the-counter marketing status.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of the type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)(x)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug and, therefore, did not require a reevaluation of the human food or target animal safety data in the parent application.

OXY-TET™ 200 Injectable Solution is under U.S. patent number 5,075,295, which expires December 12, 2009.

## VIII. APPROVED LABELING

A copy of the draft facsimile labeling is attached to this document.

- A. BIO-MYCIN® 200 - Vial Labels
- B. BIO-MYCIN® 200 - Package Inserts

32075

Lot No.:  
Exp. Date:

Each mL contains 200 mg of oxytetracycline base as oxytetracycline amphoteric.  
For the treatment of disease in beef cattle, nonlactating dairy cattle and swine.

▶ **Warning:** Discontinue treatment for at least 28 days prior to slaughter of cattle and swine. Not for use in lactating dairy animals.

**Caution:** When administered to cattle, muscle discoloration may necessitate trimming of the injection site(s) and surrounding tissues during the dressing procedure.

**Restricted Drug (California):** Use only as directed. Keep out of reach of children.

For use in animals only.

Refer to folded label attached to this container for complete directions.

**Caution:** Store at controlled room temperature, 15°-30° C (59°-86° F). Keep from freezing. Handle aseptically.

U.S. Patent No. 3,075,295

Boehringer Ingelheim Vetmedica, Inc.  
St. Joseph, MO 64506 U.S.A.

3495011-02-9808  
Code 349511



 **Boehringer  
Ingelheim**

### Bio-Mycin® 200

(oxytetracycline) Injection  
Antibiotic

200 mg/mL

ANADA 200-008, Approved by FDA

Net Contents: 100 mL

000007

32074

Lot No.:  
Exp. Date:

Each mL contains 200 mg of oxytetracycline base as oxytetracycline amphoteric.  
For the treatment of disease in beef cattle, nonlactating dairy cattle and swine.

▶ **Warning:** Discontinue treatment for at least 28 days prior to slaughter of cattle and swine. Not for use in lactating dairy animals. \*

**Caution:** When administered to cattle, muscle discoloration may necessitate trimming of the injection site(s) and surrounding tissues during the dressing procedure.

**Restricted Drug (California):** Use only as directed. Keep out of reach of children.

For use in animals only.

Refer to folded label attached to this container for complete directions.

**Caution:** Store at controlled room temperature, 15°-30° C (59°-86° F). Keep from freezing. Handle aseptically.

U.S. Patent No. 5,075,295

Boehringer Ingelheim Vetmedica, Inc.  
St. Joseph, MO 64506 U.S.A.

349519L-02-9808  
Code 349531

 **Boehringer  
Ingelheim**



**Bio-Mycin® 200**

(oxytetracycline) Injection  
Antibiotic

200 mg/mL

ANADA 200-008, Approved by FDA

Net Contents: 250 mL

800000

32073

Lot No:  
Exp. Date:

Each mL contains 200 mg of oxytetracycline base as oxytetracycline amphoteric.  
For the treatment of disease in beef cattle, nonlactating dairy cattle and swine.

**Dosage**  
**Cattle:** A single dosage of 9 mg of oxytetracycline per pound of body weight (4.5 mL/100 lb) administered *intramuscularly* or *subcutaneously* is recommended in the treatment of the following conditions: 1) bacterial pneumonia caused by *Pasteurella* spp. (shipping fever) in calves and yearlings, where retreatment is impractical due to husbandry conditions, such as cattle on range, or where repeated restraint is inadvisable; 2) infectious bovine keratoconjunctivitis (pinkeye) caused by *Moraxella bovis*.

**Swine:** A single dosage of 9 mg of oxytetracycline per pound of body weight (4.5 mL/100 lb) administered *intramuscularly* is recommended in the treatment of bacterial pneumonia caused by *Pasteurella multocida* in swine, where retreatment is impractical due to husbandry conditions or where repeated restraint is inadvisable.

▶ **Warning:** Discontinue treatment for at least 28 days prior to slaughter of cattle and swine. Not for use in lactating dairy animals. ◀

**Precautions:** Exceeding the highest recommended dosage level of drug per pound of body weight per day, administering more than the recommended number of treatments and/or exceeding 10 mL intramuscularly or subcutaneously per injection site in adult beef cattle and nonlactating dairy cattle and 5 mL intramuscularly in adult swine, may result in antibiotic residues beyond the withdrawal period.

**Caution:** When administered to cattle, muscle discoloration may necessitate trimming of the injection site(s) and surrounding tissues during the dressing procedure.

**Restricted Drug (California):** Use only as directed. Keep out of reach of children.  
For use in animals only.

Refer to folded label attached to this container for complete directions.

**Caution:** Store at controlled room temperature, 15°-30° C (59°-86° F). Keep from freezing. Handle aseptically.

U.S. Patent No. 5,075,295

Boehringer Ingelheim Vetmedica, Inc.  
St. Joseph, MO 64506 U.S.A.

349506L-03-9808  
Code 349521



Boehringer  
Ingelheim



Bio-Mycin® 200

(oxytetracycline) Injection  
Antibiotic

200 mg/mL

ANADA 200-008, Approved by FDA

Net Contents: 500 mL

000000

ANADA 200-008, Approved by FDA

## Bio-Mycin® 200

(oxytetracycline) Injection  
Antibiotic

Each mL contains 200 mg of oxytetracycline base as oxytetracycline amphoteric.

For the treatment of disease in beef cattle, nonlactating dairy cattle and swine.

Read entire insert carefully before using this product.

Bio-Mycin® 200 (oxytetracycline Injection) is a sterile, ready-to-use solution of the broad spectrum antibiotic oxytetracycline by injection. Each mL contains 200 mg of oxytetracycline base as amphoteric; magnesium oxide 1.7% w/v; sodium formaldehyde sulfoxylate 0.5% w/v; polyethylene glycol 400 30% w/v; monoethanolamine to adjust pH; water for injection USP qs. Oxytetracycline is an antimicrobial agent that is effective in the treatment of a wide range of diseases caused by susceptible gram-positive and gram-negative bacteria.

Bio-Mycin 200 does not require refrigeration; however, it is recommended that it be stored at controlled room temperature, 15°-30° C (59°-86° F). The antibiotic activity of oxytetracycline is not appreciably diminished in the presence of body fluids, serum or exudates.

**Caution:** When administered to cattle, muscle discoloration may necessitate trimming of the injection site(s) and surrounding tissues during the dressing procedure.

**Warning:** Discontinue treatment at least 28 days prior to slaughter of cattle and swine. Not for use in lactating dairy animals.

**Precautions:** Exceeding the highest recommended dosage level of drug per pound of body weight per day, administering more than the recommended number of treatments and/or exceeding 10 mL intramuscularly or subcutaneously per injection site in adult beef cattle and nonlactating dairy cattle, and 5 mL intramuscularly per injection site in adult swine, may result in antibiotic residues beyond the withdrawal period.

Reactions of an allergic or anaphylactic nature, sometimes fatal, have been known to occur in hypersensitive animals following the injection of oxytetracycline. Such adverse reactions can be characterized by signs such as restlessness, erection of hair, muscle trembling; swelling of eyelids, ears, muzzle, anus and vulva (or scrotum and sheath in males); labored breathing, defecation and urination, glassy-eyed appearance, eruption of skin plaques, frothing from the mouth, and prostration. Pregnant animals that recover may subsequently abort. At the first sign of any adverse reaction, discontinue use of this product and administer epinephrine at the recommended dosage levels. Call a veterinarian immediately.

Shock may be observed following intravenous administration, especially where highly concentrated materials are involved. To minimize this occurrence, it is recommended that Bio-Mycin 200 be administered slowly by this route.

Shortly after injection treated animals may have transient hemoglobinuria resulting in darkened urine.

As with all antibiotic preparations, use of this drug may result in overgrowth of nonsusceptible organisms, including fungi. A lack of response by the treated animal, or the development of new signs, may suggest that an overgrowth of nonsusceptible organisms has occurred. If any of these conditions occur, consult your veterinarian.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving Bio-Mycin 200 in conjunction with penicillin.

**Storage:** Store at controlled room temperature, 15°-30° C (59°-86° F). Keep from freezing.

**Care of Sick Animals:** The use of antibiotics in the management of diseases is based on an accurate diagnosis and an adequate course of treatment. When properly used in the treatment of diseases caused by oxytetracycline susceptible organisms most animals that have been treated with oxytetracycline injection show a noticeable improvement within 24 to 48 hours. It is recommended that the diagnosis and treatment of animal diseases be carried out by a veterinarian. Since many diseases look alike but require different types of treatment, the use of professional veterinary and laboratory services can reduce treatment time, costs and needless losses. Good housing, sanitation and nutrition are important in the maintenance of healthy animals, and are essential in the treatment of diseased animals.

**Intramuscular Administration:** Intramuscular injections should be made by directing the needle of suitable gauge and length into the fleshy part of a thick muscle such as in the rump, hip or thigh regions; avoid blood vessels and major nerves. Before injecting the solution, pull back gently on the plunger. If blood appears in the syringe, a blood vessel has been entered; withdraw the needle and select a different site.

No more than 10 mL should be injected intramuscularly at any one site in adult beef cattle and nonlactating dairy cattle, and not more than 5 mL per site in adult swine; rotate injection sites for each succeeding treatment. The volume administered per injection site should be reduced according to age and body size so that 1 to 2 mL per site is injected in small calves.

**Subcutaneous Administration:** Subcutaneous injections in beef cattle and nonlactating dairy cattle should be made by directing the needle of suitable gauge and length through the loose folds of the neck skin in front of the shoulder. Care should be taken to ensure that the tip of the needle has penetrated the skin but is not lodged in muscle. Before injecting the solution, pull back gently on the plunger. If blood appears in the syringe, a blood vessel has been entered; withdraw the needle and select a different site. The solution should be injected slowly into the area between the skin and muscles.

No more than 10 mL should be injected subcutaneously at any one site in adult beef cattle and nonlactating dairy cattle; rotate injection sites for each succeeding treatment. The volume administered per injection site should be reduced according to age and body size so that 1 to 2 mL per site is injected in small calves.

**Intravenous Administration:** Bio-Mycin 200 (oxytetracycline injection) may be administered intravenously to beef cattle and nonlactating dairy cattle. As with all highly concentrated materials, Bio-Mycin 200 should be administered slowly by the intravenous route.

**Preparation of the Animal for Injection:**

1. Approximate location of vein. The jugular vein runs in the jugular groove on each side of the neck from the angle of the jaw to just above the brisket and slightly above and to the side of the windpipe. (See Fig. I).
2. Restraint. A stanchion or chute is ideal for restraining the animal. With a halter, rope, or cattle leader (nose tongs), pull the animal's head around the side of the stanchion, cattle chute, or post in such a manner to form a bow in the neck (See Fig. II), then snub the head securely to prevent movement. By forming the bow in the neck, the outside curvature of the bow tends to expose the jugular vein and make it easily accessible. **Caution:** Avoid restraining the animal with a tight rope or halter around the throat or upper neck which might impede blood flow. Animals that are down present no problem as far as restraint is concerned.
3. Clip hair in area where injection is to be made (over the vein in the upper third of the neck). Clean and disinfect the skin with alcohol or other suitable antiseptic.

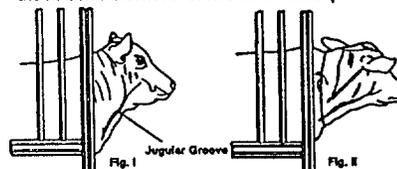


Fig. I Jugular Groove Fig. II

Entering the Vein and Making the Injection:

1. Raise the vein. This is accomplished by tying the choke rope tightly around the neck close to the shoulder. The rope should be tied in such a way that it will not come loose and so that it can be untied quickly by pulling the loose end (See Fig. II). In thick-necked animals, a block of wood placed in the jugular groove between the rope and the hide will help considerably in applying the desired pressure at the right point. The vein is a soft flexible tube through which the blood flows back to the heart. Under ordinary conditions, it cannot be seen or felt with the fingers. When the flow of blood is blocked at the base of the neck by the choke rope, the vein becomes enlarged and rigid because of the back pressure. If the choke rope is sufficiently tight, the vein stands out and can be easily seen and felt in thin-necked animals. As a further check in identifying the vein, tap it with the fingers in front of the choke rope. Pulsations that can be seen or felt with the fingers in front of the point being tapped will confirm the fact that the vein is properly distended. It is impossible to put the needle into the vein unless it is distended. Experienced operators are able to raise the vein simply by hand pressure, but the use of a choke rope is more certain.
2. Inserting the needle. This involves three distinct steps. First, insert the needle through the hide. Second, insert the needle into the vein. This may require two or three attempts before the vein is entered. The vein has a tendency to roll away from the point of the needle, especially if the needle is not sharp. The vein can be steadied with the thumb and finger of one hand. With the other hand, the needle point is placed directly over the vein, slanting it so that its direction is along the length of the vein, either toward the head or toward the heart. Properly positioned this way, a quick thrust of the needle will be followed by a spurt of blood through the needle, which indicates that the vein has been entered. Third, once in the vein, the needle should be inserted along

**Indications:** Bio-Mycin 200 is intended for use in the treatment of the following diseases in beef cattle, nonlactating dairy cattle and swine when due to oxytetracycline-susceptible organisms:

**Cattle:** In cattle, Bio-Mycin 200 is indicated in the treatment of pneumonia and shipping fever complex associated with *Pasteurella* spp. and *Haemophilus* spp.; infectious bovine keratoconjunctivitis (pink eye) caused by *Moraxella bovis*; foot-rot and diphtheria caused by *Fusobacterium necrophorum*; bacterial enteritis (scours) caused by *Escherichia coli*; wooden tongue caused by *Actinobacillus lignieresii*; leptospirosis caused by *Leptospira pomona*; and wound infections and acute metritis caused by strains of staphylococci and streptococci organisms sensitive to oxytetracycline.

**Swine:** In swine, Bio-Mycin 200 is indicated in the treatment of bacterial enteritis (scours, colibacillosis) caused by *Escherichia coli*; pneumonia caused by *Pasteurella multocida*; and leptospirosis caused by *Leptospira pomona*.

**In sows,** Bio-Mycin 200 is indicated as an aid in the control of infectious enteritis (baby pig scours, colibacillosis) in suckling pigs caused by *Escherichia coli*.

**Dosage:**

**Cattle:** Bio-Mycin 200 is to be administered by intramuscular, subcutaneous, or intravenous injection to beef cattle and nonlactating dairy cattle.

A single dosage of 9 milligrams of Bio-Mycin 200 per pound of body weight administered intramuscularly or subcutaneously is recommended in the treatment of the following conditions: 1) bacterial pneumonia caused by *Pasteurella* spp. (shipping fever) in calves and yearlings, where retreatment is impractical due to husbandry conditions, such as cattle on range, or where their repeated restraint is inadvisable; 2) infectious bovine keratoconjunctivitis (pink eye) caused by *Moraxella bovis*.

**Cattle Dosage Guide**

At the first signs of pneumonia or pink eye\* administer a single dose of Bio-Mycin® 200 by deep intramuscular injection or subcutaneous injection according to the following weight categories\*\*

Animal weight (lb)	Number of mL or cc	Animal weight (lb)	Number of mL or cc	Animal weight (lb)	Number of mL or cc
100	4.5	500	22.5	900	40.5
200	9.0	600	27.0	1000	45.0
300	13.5	700	31.5	1100	49.5
400	18.0	800	36.0	1200	54.0

\*See package insert for dosing instructions for other indicated diseases and full product information.

\*\*Do not administer more than 10 mL at any one injection site (1 to 2 mL per site in small calves).

Discontinue treatment at least 28 days prior to slaughter of cattle. Not for use in lactating dairy animals.

Bio-Mycin 200 can also be administered by intravenous, subcutaneous, or intramuscular injection at a level of 3 to 5 milligrams of oxytetracycline per pound of body weight per day. In the treatment of severe foot-rot and advanced cases of other indicated diseases, a dosage level of 5 milligrams per pound of body weight per day is recommended. Treatment should be continued 24 to 48 hours following remission of disease signs; however, not to exceed a total of four consecutive days. Consult your veterinarian if improvement is not noted within 24 to 48 hours of the beginning of treatment.

**Swine:** In swine a single dosage of 9 milligrams of Bio-Mycin 200 per pound of body weight administered intramuscularly is recommended in the treatment of bacterial pneumonia caused by *Pasteurella multocida* in swine, where retreatment is impractical due to husbandry conditions or where repeated restraint is inadvisable.

**Swine Dosage Guide**

At the first signs of pneumonia\* administer a single dose of Bio-Mycin® 200 by deep intramuscular injection according to the following weight categories\*\*

Animal weight (lb)	Number of mL or cc	Animal weight (lb)	Number of mL or cc	Animal weight (lb)	Number of mL or cc
10	0.5	125	5.6	250	11.3
25	1.1	150	6.8	275	12.4
50	2.3	175	7.9	300	13.5
75	3.4	200	9.0	325	14.6
100	4.5	225	10.1		

\*See package insert for dosing instructions for other indicated diseases and full product information.

\*\*Do not administer more than 5 mL at any one injection site.

Discontinue treatment 28 days prior to slaughter of swine.

Bio-Mycin 200 can also be administered by intramuscular injection at a level of 3 to 5 milligrams of oxytetracycline per pound of body weight per day.

Treatment should be continued 24 to 48 hours following remission of disease signs; however, not to exceed a total of four consecutive days. Consult your veterinarian if improvement is not noted within 24 to 48 hours of the beginning of treatment.

For sows, administer once intramuscularly 3 milligrams of oxytetracycline per pound of body weight approximately 8 hours before farrowing or immediately after completion of farrowing.

the length of the vein all the way to the hub, exercising caution to see that the needle does not penetrate the opposite side of the vein. Continuous steady flow of blood through the needle indicates that the needle is still in the vein. If blood does not flow continuously, the needle is out of the vein (or clogged) and another attempt must be made. If difficulty is encountered, it may be advisable to use the vein on the other side of the neck.

- While the needle is being placed in proper position in the vein, an assistant should get the medication ready so that the injection can be started without delay after the vein has been entered.
- Making the injection. With the needle in position as indicated by continuous flow of blood, release the choke rope by a quick pull on the free end. This is essential—the medication cannot flow into the vein while it is blocked. Immediately connect the syringe containing Bio-Mycin 200 (oxytetracycline injection) to the needle and slowly depress the plunger. If there is resistance to depression of the plunger, this indicates that the needle has slipped out of the vein (or is clogged) and the procedure will have to be repeated. Watch for any swelling under the skin near the needle, which would indicate that the medication is not going into the vein. Should this occur, it is best to try the vein on the opposite side of the neck.
- Removing the needle. When injection is complete, remove needle with straight pull. Then apply pressure over area of injection momentarily to control any bleeding through needle puncture, using cotton soaked in alcohol or other suitable antiseptic.

**Package Information:** Bio-Mycin 200 is available in 100-mL, 250-mL and 500-mL bottles containing 200 mg oxytetracycline per mL.

Keep out of reach of children.

U.S. Patent No. 5,075,295.

349519-02-9808

Code 349531



For swine weighing 25 lb of body weight and under, Bio-Mycin 200 should be administered undiluted for treatment at 9 mg/lb but should be administered diluted for treatment at 3 or 5 mg/lb.

Body Weight	9 MG/LB DOSAGE Volume of UNDILUTED Bio-Mycin 200		3 OR 5 MG/LB DOSAGE Volume of DILUTED Bio-Mycin 200	
	9 mg/lb	3 mg/lb	Dilution*	5 mg/lb
5 lb	0.2 mL	0.6 mL	1:7	1.0 mL
10 lb	0.5 mL	0.9 mL	1:5	1.5 mL
25 lb	1.1 mL	1.5 mL	1:3	2.5 mL

\* To prepare dilutions, add one part Bio-Mycin 200 to three, five or seven parts of sterile water; or 5 percent dextrose solution as indicated; the diluted product should be used immediately.

**Directions for Use:** Bio-Mycin 200 is intended for use in the treatment of disease due to oxytetracycline susceptible organisms in beef cattle, nonlactating dairy cattle and swine. A thoroughly cleaned, sterile needle and syringe should be used for each injection (needles and syringes may be sterilized by boiling in water for 15 minutes). In cold weather, Bio-Mycin 200 should be warmed to room temperature before administration to animals. Before withdrawing the solution from the bottle, disinfect the rubber cap on the bottle with a suitable disinfectant, such as 70% alcohol. The injection site should be similarly cleaned with the disinfectant. Needles of 16 to 18 gauge and 1 to 1 1/4 inches long are adequate for intramuscular injections. Needles 2 to 3 inches are recommended for intravenous use.

