

HFA-305

Date of Approval: APR 6 2004

FREEDOM OF INFORMATION SUMMARY

ANADA 200-356

This approval provides for the combined use of two approved Type A Medicated Articles PENNCHLOR, (chlortetracycline calcium complex equivalent to chlortetracycline hydrochloride) DENAGARD (tiamulin hydrogen fumarate), for use in the manufacture of Type B and Type C Medicated Feeds for swine.

Sponsored by:

**Pennfield Oil Company
Omaha, Nebraska 68144**

ANADA 200-356

FOIS 1

I. GENERAL INFORMATION:

- a. File Number ANADA 200-356
- b. Sponsor: Pennfield Oil Co.
14040 Industrial Rd.
Omaha, NE 68144

Drug Labeler Code: 053389
- c. Established Names: Chlortetracycline calcium complex equivalent to
Chlortetracycline HCl

Tiamulin hydrogen fumarate
- d. Proprietary Names: PENNCHLOR & DENAGARD
- e. Dosage Form: Type A Medicated Articles
- f. How Supplied: Chlortetracycline: 50-lb bags
Tiamulin hydrogen fumarate: 35-lb bags
- g. How Dispensed: OTC
- h. Amount of Active Ingredients
in Type A Medicated Article: Chlortetracycline: 50 to 100 g/lb

Tiamulin: 10 g/lb

Amount of Active Ingredients
in Type B Medicated Article: Chlortetracycline: 80,000 g/ton (40 g/lb)
Tiamulin: 7,000 g/ton (3.5 g/lb)
- i. Route of Administration: These drugs are administered orally by
adding the Type A Medicated Articles to complete
swine feed (Type B or C medicated feed).
- j. Species/Class: Swine

- k. Recommended Dosage in Type C Medicated Feeds: Chlortetracycline, 400 g/ton to provide 10 mg per pound of body weight daily
- Tiamulin: 35 g/ton
- l. Pharmacological Category: Antibacterial
- m. Indications: For treatment of swine bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline, and control of swine dysentery associated with *Brachyspira* (formerly *Serpulina* or *Treponema*) *hyodysenteriae* susceptible to tiamulin.
- n. Pioneer Products:
- AUREOMYCIN
Chlortetracycline calcium complex equivalent to Chlortetracycline hydrochloride
NADA 48-761
Alpharma, Inc.
- DENAGARD
Tiamulin hydrogen fumarate
NADA 139-472
Boehringer Ingelheim Vetmedica, Inc.
- AUREOMYCIN-DENAGARD
Chlortetracycline calcium complex equivalent to Chlortetracycline hydrochloride/
Tiamulin hydrogen fumarate
NADA 141-011
Boehringer Ingelheim Vetmedica, Inc.
- DESI "me-too"
- PENNCHLOR
Chlortetracycline calcium complex equivalent
Chlortetracycline hydrochloride
NADA 138-935
Pennfield Oil Company

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

PENNCHLOR and AUREOMYCIN were both found to comply with the results of NAS/NRC/ DESI evaluation for effectiveness as published in the FEDERAL REGISTER (61

FR 35949-35958; July 9, 1996). These products approved under the DESI "me-too" process were found to be bioequivalent at the codified level 21 CFR § 558.128(e)(3)(iv) of 10 mg/lb of body weight daily for swine.

The Center's fourth generic policy letter dated November 2, 1989, as published in the FEDERAL REGISTER on January 30, 1990 (55 FR 3107), states that the approval of a new generic Type A Medicated Article entitles the sponsor to a waiver from bioequivalence or tissue residue studies for any feed-use combinations approved for the pioneer. Since Alpharma's AUREOMYCIN is considered bioequivalent to Pennfield's PENNCHLOR, Pennfield is entitled to a bioequivalence waiver for the subject combination.

Chlortetracycline (PENNCHLOR-Pennfield) is codified under 21 CFR § 558.128(e)(3). Chlortetracycline (AUREOMYCIN-Alpharma) is codified under 21 CFR § 558.128(e)(3). Tiamulin hydrogen fumarate is codified under 21 CFR § 558.600. The combination of Tiamulin with Chlortetracycline is codified under 21 CFR § 558.600(e)(1)(iii) and the NADA 141-011 was approved on August 20, 1996.

3. HUMAN SAFETY:

• Tolerances for Residues:

The tolerances established for the pioneer product apply to the generic product.

Tolerances for the sums of residues of tetracycline, including chlortetracycline in tissues of swine, are as follows: (a) 2 parts per million (ppm) in muscle; (b) 6 ppm in liver; (c) 12 ppm in fat and kidneys (21 CFR § 556.150). The acceptable daily intake for residues of chlortetracycline is 25 micrograms per kilogram of body weight per day.

Under NADA 141-011, a tolerance for tiamulin of 0.6 part per million was established for 8-*alpha*-hydroxymutilin (marker compound) in liver (target tissue) of swine (21 CFR 556.738).

• Withdrawal Times:

The assigned withdrawal period is the same as the pioneer product.

Based on the limitation in 21 CFR § 558.600(e)(1)(iii), a 2 day withdrawal time is required for the combination of chlortetracycline and tiamulin.

• Regulatory Methods for Residues:

The regulatory analytical method for the determination of residue of chlortetracycline 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.

An approved regulatory method was used for determining the tiamulin marker residue, 8-*alpha*-hydroxymutilin, in swine liver. This method involves extraction, derivation, and then quantitation by gas chromatography. The limit of quantitation (LOQ) is 50 parts per billion. This method is on file at the Center for Veterinary Medicine, Food and Drug Administration, HFV-199, 7500 Standish Place, Rockville, MD 20855.

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512 (n) of the act and demonstrates that the combination of chlortetracycline and tiamulin hydrogen fumarate when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached below:

Type B and Type C Medicated Feed (Blue Bird) – Generic Labeling for
ANADA 200-356

Type B and Type C Medicated Feed (Blue Bird) – Pioneer Labeling for NADA 141-011

PennField

NET WEIGHT: 50 lb (22.68 kg) Bag

**BLUE BIRD
(TYPE B MEDICATED FEED)**

4

For preparing complete swine feed.

STARTER-GROWER-FINISHER FEEDS

For the control of swine dysentery associated with *Serpulina hyodysenteriae* susceptible to tiamulin and for treatment of swine bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* sensitive to chlortetracycline and treatment of bacterial pneumonia caused by *Pasteurella multocida* sensitive to chlortetracycline.

ACTIVE INGREDIENTS

Tiamulin (as hydrogen fumarate)	7,000 g/ton (3.5 g/lb)
Chlortetracycline calcium complex equivalent to chlortetracycline HCl	80,000 g/ton (40 g/lb)

GUARANTEED ANALYSIS

INGREDIENTS

WARNING

Withdraw medicated feed 2 days before slaughter.

CAUTION

1. For use in swine only. Not for use in swine weighing over 250 lbs.
2. Swine being treated with tiamulin should not have access to feeds containing polyether ionophores (e.g., monensin, salinomycin, narasin, semduramicin and lasalocid) as adverse reactions may occur.
3. If signs of toxicity occur, discontinue use of medicated feed.

MIXING DIRECTIONS

Mix 10 pounds of this Type B Medicated Feed with 1990 pounds of nonmedicated swine feed to make a complete ration containing 35 g tiamulin hydrogen fumarate and 400 g chlortetracycline per ton.

USE DIRECTIONS

Feed continuously as the sole ration for 14 days.

For Use In Animals Only.

PROTECT FROM EXCESSIVE TEMPERATURES (TEMPERATURES THAT EXCEED 40°C OR 104°F). DO NOT STORE AT WARM TEMPERATURES UP TO 104°F (40°C) FOR MORE THAN 7 DAYS.

Manufactured by
BLUE BIRD FEED COMPANY
Robin, Indiana 99999

PennField

NET WEIGHT: Bulk or 100 lb (45.4 kg) Bag

**BLUE BIRD
(TYPE C MEDICATED FEED)**

STARTER-GROWER-FINISHER FEEDS

For the control of swine dysentery associated with *Serpulina hyodysenteriae* susceptible to tiamulin and for treatment of swine bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* sensitive to chlortetracycline and treatment of bacterial pneumonia caused by *Pasteurella multocida* sensitive to chlortetracycline.

ACTIVE INGREDIENTS

Tiamulin hydrogen fumarate	35 g/ton
Chlortetracycline calcium complex equivalent to chlortetracycline HCl	Approximately 400 g/ton varying with body weight and feed consumption to provide 10 mg/lb body weight daily.

GUARANTEED ANALYSIS

Crude protein, not less than	_____ %
Crude fat, not less than	_____ %
Crude fiber, not more than	_____ %

INGREDIENTS

Each ingredient must be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions adopted by AAFCO.

WARNING

Withdraw medicated feed 2 days before slaughter.

CAUTION

Do not feed to animals other than swine. Not for use in swine weighing over 250 lbs. Swine being treated with tiamulin should not have access to feeds containing polyether ionophores (e.g., monensin, salinomycin, narasin, semduramicin and lasalocid) as adverse reactions may occur. If signs of toxicity occur, discontinue use of medicated feed.

For Use In Animals Only.

PROTECT FROM EXCESSIVE TEMPERATURES (TEMPERATURES THAT EXCEED 40°C OR 104°F). DO NOT STORE AT WARM TEMPERATURES UP TO 104°F (40°C) FOR MORE THAN 7 DAYS.

Manufactured by
BLUE BIRD FEED COMPANY
Robin, Indiana 99999

FERMENTA

NET WEIGHT: 50 lb (22.68 kg) Bag

BLUE BIRD
(TYPE B MEDICATED FEED)

For preparing complete swine feed.

STARTER-GROWER-FINISHER FEEDS

For the control of swine dysentery associated with *Serpulina hyodysenteriae* susceptible to tiamulin and for treatment of swine bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* sensitive to chlortetracycline and treatment of bacterial pneumonia caused by *Pasteurella multocida* sensitive to chlortetracycline.

ACTIVE INGREDIENTS

Tiamulin (as hydrogen fumarate)	7,000 g/ton (3.5 g/lb)
Chlortetracycline calcium complex equivalent to chlortetracycline HCl	80,000 g/ton (40 g/lb)

GUARANTEED ANALYSIS

INGREDIENTS

WARNING

Withdraw medicated feed 2 days before slaughter.

CAUTION

1. For use in swine only. Not for use in swine weighing over 250 lbs.
2. Swine being treated with tiamulin should not have access to feeds containing polyether ionophores (e.g., monensin, salinomycin, narasin, semduramicin and lasalocid) as adverse reactions may occur.
3. If signs of toxicity occur, discontinue use of medicated feed.

MIXING DIRECTIONS

Mix 10 pounds of this Type B Medicated Feed with 1990 pounds of nonmedicated swine feed to make a complete ration containing 35 g tiamulin hydrogen fumarate and 400 g chlortetracycline per ton.

USE DIRECTIONS

Feed continuously as the sole ration for 14 days.

For Use In Animals Only.

PROTECT FROM EXCESSIVE TEMPERATURES (TEMPERATURES THAT EXCEED 40°C OR 104°F). DO NOT STORE AT WARM TEMPERATURES UP TO 104°F (40°C) FOR MORE THAN 7 DAYS.

Manufactured by
BLUE BIRD FEED COMPANY
Robin, Indiana 99999

FERMENTA

NET WEIGHT: Bulk or 100 lb (45.4 kg) Bag

BLUE BIRD
(TYPE C MEDICATED SWINE FEED)

STARTER-GROWER-FINISHER FEEDS

For the control of swine dysentery associated with *Serpulina hyodysenteriae* susceptible to tiamulin and for treatment of swine bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* sensitive to chlortetracycline and treatment of bacterial pneumonia caused by *Pasteurella multocida* sensitive to chlortetracycline.

ACTIVE DRUG INGREDIENTS

Tiamulin hydrogen fumarate----- 35 g/ton

Chlortetracycline calcium complex
equivalent to chlortetracycline HCl----- Approximately 400 g/ton
varying with body weight and
and feed consumption to provide
10 mg/lb. body weight daily

GUARANTEED ANALYSIS

Crude protein, not less than _____ %
Crude fat, not less than _____ %
Crude fiber, not more than _____ %

INGREDIENTS

Each ingredient must be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions adopted by AAFCO.

DIRECTIONS FOR USE

Feed continuously as the sole ration for not more than 14 days.

WARNING

Withdraw medicated feed 2 days before slaughter.

CAUTION

Do not feed to animals other than swine. NOT for use in swine weighing over 250 pounds. Swine being treated with tiamulin should not have access to feeds containing polyether ionophores (e.g. monensin, salinomycin, narasin, sanduramycin and lasalocid) as adverse reactions may occur. If signs of toxicity occur, discontinue use of medicated feed.

For Use In Animals Only.

PROTECT FROM EXCESSIVE TEMPERATURES (TEMPERATURES THAT EXCEED 40°C OR 104°F). DO NOT STORE AT WARM TEMPERATURES UP TO 104°F (40°C) FOR MORE THAN 7 DAYS.

Manufactured by
BLUE BIRD FEED COMPANY
Robin, Indiana 49969