Date of Approval: May 7, 2019

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-633

Denagard® and Deracin®

tiamulin hydrogen fumarate and chlortetracycline

Type A medicated articles to be used in the manufacture of Type C medicated feeds

Swine

Original abbreviated new animal drug approval of a medicated feed combination for the indications listed in Section I.L

Sponsored by:

Pharmgate Inc.

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I. GENERAL INFORMATION

A. File Number

ANADA 200-633

B. Sponsor

Pharmgate Inc.
1800 Sir Tyler Dr.,
Wilmington, NC 28405

Drug Labeler Code: 069254

C. Proprietary Name

Denagard® and Deracin®

D. Drug Product Established Name

tiamulin hydrogen fumarate and chlortetracycline

E. Pharmacological Categories

Denagard®: Antimicrobial
Deracin®: Antimicrobial

F. Dosage Form

Type A medicated articles for use in the manufacture of Type C medicated feeds.

G. Amount of Active Ingredients in Currently Marketed Products[1]

Denagard®: 363.2 grams per pound of tiamulin hydrogen fumarate
Deracin®: 50 to 100 grams per pound of chlortetracycline

H. How Supplied

Denagard® (tiamulin hydrogen fumarate): 55 lb bag
Deracin® (chlortetracycline): 50 lb bag

I. Dispensing Status

VFD

J. Route of Administration

Oral, in feed

[1] The sponsors of these individual currently marketed Type A medicated articles may have approvals for other strengths of these products that are for use in the same species and class, for the same indications, and at the same dosages, but are not currently marketing those strengths of these Type A medicated articles. Such strengths, when legally marketed, are also approved for use in the manufacture of [Type B and] Type C medicated feeds that are the subject of this approval.

K. Species/Class

Swine

L. Indications and Dosage Regimens

1. For control of swine dysentery associated with *Brachyspira* (formerly *Serpulina* or *Treponema*) *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.

    a. 35g/ton of Denagard® in finished Type C medicated feed for control of swine dysentery associated with *Brachyspira* (formerly *Serpulina* or *Treponema*) *hyodysenteriae* susceptible to tiamulin.

    b. Approximately 400g/ton of Deracin® in finished Type C medicated feed for the 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.

    Feed continuously as the sole ration for 14 days.

M. Reference Listed New Animal Drug Combination

Denagard® (tiamulin hydrogen fumarate) plus CTC (chlortetracycline); NADA 141-011; Elanco US Inc.

N. Approved Original Generic Type A Medicated Article

Deracin® (chlortetracycline); ANADA 200-510; Pharmgate Inc.

O. Individual Type A medicated articles approved for use in the manufacture of the Type C combination medicated feeds in this application

Denagard® (tiamulin hydrogen fumarate); NADA 139-472; Elanco US Inc.
Deracin® (chlortetracycline); ANADA 200-510; Pharmgate Inc.

II. BIOEQUIVALENCE

Under the provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

According to CVM's fourth policy letter issued on November 2, 1989, with regard to the implementation of GADPTRA, after the approval of an ANADA for a generic Type A medicated article, the generic sponsor is entitled to approval for all the feed-mixed combinations for which the RLNAD is approved. Bioequivalence and tissue residue studies are not required for the approval of the generic feed use combinations (Type B or C medicated feeds). Chlortetracycline is codified under 21 CFR 558.128

and tiamulin hydrogen fumarate is codified under 21 CFR 558.612. The combination of chlortetracycline and tiamulin hydrogen fumarate is codified under 21 CFR 558.128.

III. EFFECTIVENESS

CVM did not require effectiveness studies for this approval.

IV. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this approval.

V. HUMAN FOOD SAFETY

The following are assigned to this product for swine:

A. Acceptable Daily Intake and Tolerances for Residues

The acceptable daily intake (ADI) for total residues of tetracyclines including chlortetracycline, oxytetracycline, and tetracycline is 25 micrograms *per* kilogram of body weight *per* day. The ADI for total residues of tiamulin is 25 micrograms *per* kilogram of body weight *per* day. The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product. A tolerance of 2 parts *per* million is established for tetracyclines in muscle, 6 ppm in liver, and 12 ppm in fat and kidney, under 21 CFR 556.150. A tolerance of 0.6 ppm is established for 8-alpha-hydroxymutilin (the marker residue) in liver (the target tissue), under 21 CFR 556.732.

B. Withdrawal Period

Because a waiver from the requirement to perform *in vivo* bioequivalence studies was granted for the Type A medicated article Deracin®, the withdrawal periods for the combination Type C medicated feeds are those previously assigned to the RLNAD product. When used together, chlortetracycline and tiamulin hydrogen fumarate are approved with a 2-day withdrawal period.

C. Analytical Methods for Residues

The validated analytical methods for analysis of residues of chlortetracycline and tiamulin hydrogen fumarate are on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855. To obtain copies of the analytical methods, please submit a Freedom of Information request to: https://www.accessdata.fda.gov/scripts/foi/FOIRequest/requestinfo.cfm.

VI. USER SAFETY

CVM did not require user safety studies for this original approval. There are no user safety warnings on the Type C medicated feed label.

VII. AGENCY CONCLUSIONS

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the FD&C Act and demonstrates that Denagard® and Deracin®, when used according to the label, are safe and effective.

Additionally, data demonstrate that residues in food products derived from species administered Denagard® and Deracin® will not represent a public health concern when the combination medicated feed is used according to the label.