Date of Approval: February 28, 2018

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-483

Deccox® and LINCOMIX®

(decoquinate Type A medicated article and lincomycin Type A medicated article)

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

Broiler chickens

Original approval of an Animal Drug and Availability Act (ADAA) of 1996 feed combination for the indications listed in Section I.L.

Sponsored by:

Zoetis Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 141-483

B. Sponsor

Zoetis Inc.
333 Portage St.
Kalamazoo, MI 49007

Drug Labeler Code: 054771

C. Proprietary Name

Deccox® and LINCOMIX®

D. Product Established Names

decoquinate Type A medicated article and lincomycin Type A medicated article

E. Pharmacological Category

Deccox®: coccidiostat
LINCOMIX®: antimicrobial

F. Dosage Form

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

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

Deccox®: 27.2 g/lb of decoquinate
LINCOMIX®: 20 or 50 g/lb of lincomycin (as lincomycin hydrochloride agricultural grade)

H. How Supplied

Deccox®: 50 lb bag
LINCOMIX®: 50 lb bag

I. Dispensing Status

VFD

[1] The sponsors of these individual currently marketed Type A medicated articles may have approvals for other strengths 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 C medicated feeds that are the subject of this approval.

J. Route of Administration

Oral

K. Species/Class

Broiler chickens

L. Indication and Dosage Regimen

For the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. maxima, E. mivati,* and *E. brunetti*, and for the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to lincomycin in broiler chickens.

1. 27.2 g/ton of Deccox® for the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. maxima, E. mivati*, and *E. brunetti.*

2. 2 g/ton of LINCOMIX® for the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to lincomycin.

Feed as the sole ration to broiler chickens.

II. EFFECTIVENESS

In accordance with the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the ADAA of 1996, if the animal drugs or active ingredients intended for use in combination in an animal feed have already been separately approved for the particular uses and conditions for which they are intended for use in combination, the Center for Veterinary Medicine (CVM) will not refuse to approve an NADA for the combination on effectiveness grounds unless the FDA finds that the sponsor fails to demonstrate that:

- there is substantial evidence to indicate that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the proposed combination makes a contribution to the labeled effectiveness
- each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population
- where the combination contains more than one nontopical antibacterial active ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial active ingredients or animal drugs makes a contribution to the labeled effectiveness.

Decoquinate Type A medicated article, as provided by Zoetis Inc., has previously been separately approved for use in feed for broiler chickens for the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. maxima, E. mivati, and E. brunetti.* (21 CFR 558.195). Lincomycin Type A medicated article, as provided by Zoetis Inc., has previously been separately approved for use in feed for broiler chickens for the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to lincomycin (21 CFR 558.325). Effectiveness of each drug, decoquinate Type A medicated article and lincomycin Type A medicated article,

when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Zoetis Inc.'s approved NADAs 039-417 and 097-505 for decoquinate Type A medicated article and lincomycin Type A medicated article, respectively.

Because decoquinate Type A medicated article and lincomycin Type A medicated article each have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that decoquinate Type A medicated article plus lincomycin Type A medicated article provide appropriate concurrent use for the intended target population. The use of decoquinate Type A medicated article plus lincomycin Type A medicated article provides appropriate concurrent use because these drugs are intended to treat different conditions (prevention of coccidiosis and control of necrotic enteritis, respectively) likely to occur simultaneously with sufficient frequency in broiler chickens. There is no more than one nontopical antibacterial contained in this combination animal drug intended for use in Type C medicated feed.

III. TARGET ANIMAL SAFETY

In accordance with the FD&C Act, as amended by the ADAA of 1996, if the animal drugs or active ingredients intended for use in combination in animal feed have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, CVM will not refuse to approve an NADA for the combination on target animal safety grounds unless:

- there is a substantiated scientific issue specific to an active ingredient or animal drug used in the combination that cannot adequately be evaluated based on the information contained in the application for the combination, and CVM finds that the application fails to show that the combination is safe, or
- there is a scientific issue raised by target animal observations contained in the studies submitted to the NADA for the combination, and CVM finds that the application fails to show that the combination is safe.

Decoquinate Type A medicated article, as provided by Zoetis Inc., has previously been separately approved for use in feed for broiler chickens for the prevention of coccidiosis in broiler chickens - caused by *Eimeria tenella, E. necatrix, E. acervulina, E. maxima, E. mivati, and E. brunetti.* (21 CFR 558.195). Lincomycin Type A medicated article, as provided by Zoetis Inc., has previously been separately approved for use in feed for broiler chickens for the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to lincomycin (21 CFR 558.325).

Under the provisions of ADAA, this original approval allows for the combination of decoquinate Type A medicated article (as provided by Zoetis Inc.) and lincomycin Type A medicated article (as provided by Zoetis Inc.). Target animal safety for each drug, decoquinate Type A medicated article and lincomycin Type A medicated article, when administered alone in accordance with its approved uses and conditions of use is demonstrated in Zoetis Inc.'s approved NADAs 039-417 and 097-505 for decoquinate Type A medicated article and lincomycin Type A medicated article, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of decoquinate Type A medicated article and lincomycin Type A

medicated article when used in combination under this NADA and no scientific issue has been raised by target animal observations submitted as part of the NADA for this combination. Therefore, in accordance with the FD&C Act, as amended by the ADAA of 1996, no specific target animal safety studies are required for approval of this application.

IV. HUMAN FOOD SAFETY

In accordance with the FD&C Act, as amended by the ADAA of 1996, if the animal drugs or active ingredients intended for use in combination in animal feed have already been separately approved for the particular uses and conditions of use for which they are intended for use in combination, CVM will not refuse to approve an NADA for the combination on human food safety grounds unless CVM finds that the application fails to establish that:

- none of the active ingredients or animal drugs used in combination at the longest withdrawal for any of the active ingredients or animal drugs in the combination exceeds the established tolerance, or
- none of the active ingredients or animal drugs in combination interferes with the method of analysis for another active ingredient or animal drug in the combination.

A. Toxicology

Safety of the individual drugs in this combination product has been established by data in NADA 039-417 for decoquinate (FR Vol. 35 No. 35 pg. 3162, dated February 19, 1970) and NADA 111-636 for lincomycin (FOI Summary dated January 23, 1990).

B. Residue Chemistry

1. Summary of Residue Chemistry Studies

   a. Total Residue and Metabolism Studies

      CVM did not require total residue and metabolism studies for this approval. NADA 039-417 contains summaries of studies supporting the approval of decoquinate in broiler chickens (FR Vol. 35 No. 35 pg. 3162, dated February 19, 1970). NADA 097-505 contains summaries of studies supporting the approval of lincomycin in broiler chickens (FR Vol. 35 No. 91 pg. 7300, dated May 9, 1970).

   b. Comparative Metabolism Studies

      CVM did not require comparative metabolism studies for this approval. NADA 039-417 contains studies supporting the approval of decoquinate in broiler chickens (FR Vol. 35 No. 35 pg. 3162, dated February 19, 1970). NADA 097-505 contains studies supporting the approval of lincomycin in broiler chickens (FR Vol. 35 No. 91 pg. 7300, dated May 9, 1970).

c. Tissue Residue Depletion Study

For ADAA combination approvals, the FD&C Act [section 512(d)(4)(A)] only permits the Agency to evaluate whether any active ingredients or drugs, at the longest withdrawal period for either active ingredient or drug, exceeds its established tolerance. Therefore, because a tolerance for lincomycin is not required in edible chicken tissues (21 CFR 556.360), there is no requirement to assess the effect of decoquinate on the depletion or assay of lincomycin residues in edible chicken tissues in support of this approval. The Agency did evaluate a study that assessed the effect of lincomycin on the depletion and assay of decoquinate residues in edible tissues of chickens.

Study Title: To Determine if Feeding the Combination of Lincomycin and Decoquinate Results in Residues of These Drugs in Chicken Broiler Tissue (Report Number: CHM 70:58)

In-life Animal Phase Study Location: Ashland, OH, USA

Analytical Phase Study Location: Ashland, OH, USA and Kalamazoo, MI, USA

Study Completion Date: November 5, 1970

Objective: The objective of this study was to determine the concentration of lincomycin and decoquinate residues in edible tissues of chickens fed 4 g/ton lincomycin and 27.2 g/ton decoquinate in a Type C medicated feed.

Four groups of 100 chickens each (50 males, 50 females) were used in this study (Table IV.1). Group 1 chickens were fed unmedicated feed for 56 days. Group 2 chickens were fed a Type C medicated feed containing 4 g/ton lincomycin for 56 days. Group 3 chickens were fed a Type C medicated feed containing 27.2 g/ton decoquinate for 56 days. Group 4 chickens were fed a Type C medicated feed containing 4 g/ton lincomycin and 27.2 g/ton decoquinate for 56 days.

Table IV.1. Groups and inclusion rates for lincomycin and decoquinate

Group	Lincomycin feed concentration	Decoquinate feed concentration
1	0 g/ton	0 g/ton
2	4 g/ton	0 g/ton
3	0 g/ton	27.2 g/ton
4	4 g/ton	27.2 g/ton

Three male and three female chickens were slaughtered from Group 1, Group 2, Group 3, and Group 4 at 0-day withdrawal from medicated feed. In addition, three female chickens from Group 3 and three male and three female chickens from Group 4 were slaughtered one day after being withdrawn from medicated feed. Muscle, skin with fat, liver and kidney tissues were collected from these chickens and analyzed for decoquinate concentration by column chromatography followed by fluorometric

detection (Table IV.2).

Table IV.2. Mean (± standard deviation) decoquinate concentrations in tissues from broiler chickens fed unmedicated feed (Group 1); feed containing lincomycin, (Group 2); feed containing decoquinate (Group 3); or feed containing lincomycin and decoquinate (Group 4).

Group	Days Withdrawn from Medicated Feed	Muscle Decoquinate Concentration (ppm)	Skin with Fat Decoquinate Concentration (ppm)	Liver Decoquinate Concentration (ppm)	Kidney Decoquinate Concentration (ppm)
1	0	negligible	negligible	negligible	negligible
2	0	negligible	negligible	negligible	negligible
3	0	0.28 ± 0.06	1.07 ± 0.36	1.06 ± 0.15	0.81 ± 0.03
4	0	0.21 ± 0.10	0.88 ± 0.11	0.97 ± 0.16	0.80 ± 0.11
3	1	0.04 ± 0.03	0.60 ± 0.27	0.43 ± 0.12	0.31 ± 0.05
4	1	0.10 ± 0.07	0.70 ± 0.40	0.46 ± 0.06	0.35 ± 0.07

The effects of lincomycin on the assay of decoquinate was assessed. Decoquinate (0 to 5 µg) was added to control tissue, and the mixture was assayed in presence and absence of lincomycin (0 or 10 µg). The decoquinate assay results were similar between the samples containing lincomycin and the samples without lincomycin.

2. Target Tissue and Marker Residue Assignment

   A target tissue is not assigned for decoquinate. NADA 039-417 contains studies supporting the approval of decoquinate in broiler chickens (FR Vol. 35 No. 35 pg. 3162, dated February 19, 1970). These studies established decoquinate as the marker residue (21 CFR 556.170).

   A target tissue and marker residue are not assigned for lincomycin in edible chicken tissues (21 CFR 556.360).

3. Tolerance Assignments

   NADA 039-417 contains studies supporting the approval of decoquinate in broiler chickens (FR Vol. 35 No. 231 pg.18194, dated November 28, 1970). These studies established a tolerance of 1 part per million (ppm) in muscle tissue and 2 ppm in other edible chicken tissues for residues of decoquinate (21 CFR 556.170).

   A tolerance for residues of lincomycin is not required in edible chicken tissues (FR Vol. 55 No. 21 pg. 3208, dated January 31, 1990; 21 CFR 556.360).

4. Withdrawal Period

   A 0-day withdrawal period is assigned for the combined use of Deccox® and LINCOMIX® when fed to broiler chickens as a Type C medicated feed containing 27.2 g/ton decoquinate and 2 g/ton lincomycin.

C. Microbial Food Safety

1. Antimicrobial Resistance

   With respect to the human food safety evaluation for these types of combination new animal drug approvals, the Agency is permitted only to evaluate whether any active ingredient or drug intended for use in the combination exceeds its established tolerance at the longest withdrawal time of any of the active ingredients or drugs in the combination, and whether any of the active ingredients or drugs of the combination interferes with the methods of analysis of another active ingredient or drug in the combination [section 512(d)(4)(A) of the FD&C Act]. Therefore, the effect of this combination of decoquinate and lincomycin on antimicrobial resistance among bacteria of public health concern in or on treated broiler chickens was not assessed.

2. Impact of Residues on Human Intestinal Flora

   With respect to the human food safety evaluation for these types of combination new animal drug approvals, the Agency is permitted only to evaluate whether any active ingredient or drug intended for use in the combination exceeds its established tolerance at the longest withdrawal time of any of the active ingredients or drugs in the combination, and whether any of the active ingredients or drugs of the combination interferes with the methods of analysis of another active ingredient or drug in the combination [section 512(d)(4)(A) of the FD&C Act]. Therefore, the effect of this combination of decoquinate and lincomycin on the human intestinal flora was not assessed.

D. Analytical Method for Residues

1. Determinative Method

   An analytical method for decoquinate is described in NADA 039-417.

   Because a tolerance for residues of lincomycin is not required for edible chicken tissues, an analytical method is not required.

2. Availability of Method

   The method is available from CVM, FDA, 7500 Standish Place, Rockville, MD 20855. To obtain a copy of the analytical method, please submit a Freedom of Information Summary request to: https://www.accessdata.fda.gov/scripts/foi/FOIRequest/requestinfo.cfm.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to the Type C medicated feed:

Not for use in humans. Keep out of reach of children.

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the FD&C Act and 21 CFR part 514. The data contained in the previously approved NADAs for Deccox® and LINCOMIX® demonstrate that, when they are used according to the label, they are safe and effective for the prevention of coccidiosis caused by *Eimeria tenella, E. necatrix, E. acervulina, E. maxima, E. mivati,* and *E. brunetti,* and for the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to lincomycin in broiler chickens. Additionally, data demonstrate that residues in food products derived from broiler chickens treated with Deccox® and LINCOMIX® will not represent a public health concern when the product is used according to the label.

A. Marketing Status

A valid veterinary feed directive (VFD) is required to dispense this drug. Any animal feed bearing or containing this drug will be fed to animals only by or on a lawful VFD issued by a licensed veterinarian in the course of their professional practice. In addition, the VFDs issued for this drug are not refillable.

Labeling restricts this drug to use under the professional supervision of a licensed veterinarian. The decision to restrict this drug to use by or upon a lawful VFD issued by a licensed veterinarian was based on the following factors: (a) adequate directions cannot be written to enable lay persons to appropriately and safely use this product and (b) restricting this drug to use by or upon a lawful VFD issued by a licensed veterinarian should help prevent indiscriminate use, which could result in violative tissue residues.

B. Exclusivity

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(ii) of the FD&C Act.

C. Patent Information

For current information on patents, see the Animal Drugs @ FDA database or the Green Book on the FDA CVM internet website.