Date of Approval: February 26, 2021

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-540

Pennitracin MD® and Coban™

(bacitracin Type A medicated article) and
(monensin Type A medicated article)

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

Growing turkeys

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

Sponsored by:

Pharmgate, Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 141-540

B. Sponsor

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

Drug Labeler Code: 069254

C. Proprietary Names

Pennitracin MD® and Coban™

D. Drug Product Established Names

bacitracin Type A medicated article and monensin Type A medicated article

E. Pharmacological Categories

Pennitracin MD®: antimicrobial
Coban™: anticoccidial

F. Dosage Form

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

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

Pennitracin MD®: 50 g/lb bacitracin (as feed grade bacitracin methylenedisalicylate)
Coban™: 90.7 g/lb monensin, USP

H. How Supplied

Pennitracin MD®: 50 lb bag
Coban™: 55.12 lb bag

I. Dispensing Status

Over-the-counter (OTC)

[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

Growing turkeys

L. Indication and Dosage Regimen

1. For increased rate of weight gain and improved feed efficiency, and for the prevention of coccidiosis caused by *Eimeria adenoeides*, *E. meleagrimitis* and *E. gallopavonis* in growing turkeys

   a. 4 to 50 g/ton of bacitracin (as feed grade bacitracin methylenedisalicylate provided by Pennitracin MD®) for increased rate of weight gain and improved feed efficiency

   b. 54 to 90 g/ton of monensin (as Coban™) for the prevention of coccidiosis caused by *Eimeria adenoeides*, *E. meleagrimitis* and *E. gallopavonis*

   Feed continuously as the sole ration. The optimum level depends upon the severity of coccidiosis exposure.

II. EFFECTIVENESS AND TARGET ANIMAL SAFETY

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the ADAA of 1996, allows for drugs to be fed in combination in or on medicated feed without additional demonstration of their effectiveness or target animal safety when certain conditions are met. In those cases, the FD&C Act provides that effectiveness and target animal safety of each drug, demonstrated in its NADA at the time of the approval, are adequate. The Agency has based its determination of the effectiveness and target animal safety of the combination of bacitracin Type A medicated article and monensin Type A medicated article on the effectiveness and target animal safety of the previously separately approved conditions of use for Pennitracin MD® and Coban™ for use in growing turkeys, respectively, as these drugs or their active ingredients intended for use in combination in animal feeds have met the following criteria:

- 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;
- there was not a substantiated scientific issue specific to an active ingredient or animal drug used in the combination that was not adequately evaluated based on the information contained in the application for the combination, and no data presented in the application raised a safety concern with the Agency; and

- there was not a scientific issue raised by target animal observations contained in the studies submitted to the NADA for the combination, and no data presented in the application raised a safety concern with the Agency.

Effectiveness and target animal safety of the individual drugs in this combination has been established by data in the following NADAs (refer to Table II.1):

Table II.1. Summary of effectiveness and target animal safety for the individual drugs subject to this combination.

Drug Product	Indication	Approval Information
Pennitracin MD® Sponsored by Pharmgate, Inc.	For use in feeds for broiler and replacement chickens, growing turkeys or growing pheasants for increased rate of weight gain and improved feed efficiency.	NADA 141-137 (21 CFR 558.76(e)(1)(ii))
Coban™* Sponsored by Elanco US Inc.	For use in feeds for growing turkeys for the prevention of coccidiosis caused by *Eimeria adenoeides*, *E. meleagrimitis* and *E. gallopavonis*.	NADA 130-736 (as published in the FEDERAL REGISTER (52 FR 15718) on April 30, 1987; and the FOI Summary, dated March 23, 1990[a])

* Elanco US Inc. has provided Pharmgate, Inc. right of reference to use Coban™ in this combination.

[a] The FOI Summary, dated March 23, 1990, contained additional target animal safety information but relied on the effectiveness information from the original approval.

III. HUMAN FOOD SAFETY

With respect to the human food safety evaluation for these types of combination new animal drug approvals, the Agency evaluates 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, only additional residue chemistry data and assay noninterference information were needed to support approval of this ADAA feed-use combination. The Agency has based its determination of the human food safety of the combination of bacitracin methylenedisalicylate and monensin on the human food safety of the previously separately approved conditions of use for Pennitracin MD® and Coban™ for use in turkeys, respectively, as these drugs or their active ingredients intended for use in combination in animal feeds have met the following criteria:

- 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, and
- 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. Microbial Food Safety

As noted, Section 512(d)(4)(A) of the FD&C Act limits CVM's human food safety evaluation for these types of ADAA feed-use combination new animal drug approvals; therefore, microbial food safety was not assessed.

B. Toxicology

As noted, Section 512 (d)(4)(A) of the FD&C Act limits CVM's human food safety evaluation for these types of ADAA feed-use combination new animal drug approvals; therefore, toxicology assessment of these types of combination new animal drugs was not performed. Safety of the individual drugs in this combination has been established by data in the following NADAs (refer to Table III.1.):

Table III.1. Toxicology assessment of the individual drugs in this combination.

Drug Product	Approval Information
Pennitracin MD®	NADA 141-137 (as published in the FEDERAL REGISTER (80 FR 79474) on December 22, 2015)
Coban™	NADA 130-736 (as published in the FEDERAL REGISTER (52 FR 15718) on April 30, 1987)

C. 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 141-137 contains summaries of studies supporting the approval of bacitracin methylenedisalicylate in turkeys (80 FR 79474, dated December 22, 2015). The sponsor obtained a right of reference to data in the NADA 130-736 file to support this approval. NADA 130-736

contains a summary of studies supporting the approval of monensin in turkeys (52 FR 15718, dated April 30, 1987).

b. Comparative Metabolism Study

CVM did not require comparative metabolism studies for this approval. NADA 141-137 contains summaries of studies supporting the approval of bacitracin methylenedisalicylate in turkeys (80 FR 79474, dated December 22, 2015). The sponsor obtained a right of reference to data in the NADA 130-736 file to support this approval. NADA 130-736 contains a summary of studies supporting the approval of monensin in turkeys (52 FR 15718, dated April 30, 1987).

c. Tissue Residue Depletion Study

In lieu of conducting a tissue residue depletion study, the sponsor obtained a right of reference to data and information in the NADA 140-937 file (approved combination of BMD® and Coban™ for use in the manufacture of Type C medicated feed for turkeys) to support this approval. CVM considered Pennitracin MD® and BMD® as equal with respect to human food safety for this approval. CVM relied on the tissue residue depletion study (Study No. AAC8722), titled, "Tissue residue interference study in turkeys medicated with bacitracin methylene disalicylate (200 g/ton) and monensin (90 g/ton) in feed" in the NADA 140-937 file to demonstrate tissue residue depletion noninterference and assay noninterference for this approval, and to reach the conclusion that the combination of Pennitracin MD® and Coban™ for use in the manufacture of Type C medicated feed for growing turkeys (4 to 50 g bacitracin methylenedisalicylate/ton and 54 to 90 g monensin/ton of feed) qualifies for a zero-day withdrawal period assignment. Study No. AAC8722 was described in the FOI Summary for the original approval of NADA 140-937 dated November 8, 1994. A brief summary of the study is provided below to show how the residue data from that study were used to support this approval:

Study Title: "Tissue residue interference study in turkeys medicated with bacitracin methylene disalicylate (200 g/ton) and monensin (90 g/ton) in feed" - Study No. AAC8722

Study Design: In the study, 5 male and 5 female turkeys were fed medicated feed containing 200 g bacitracin methylene disalicylate/ton and 90 g monensin/ton of feed for 27 days. The animals were slaughtered at 6 hours (zero withdrawal) following withdrawal of the medicated feed. Tissue samples were collected after the slaughter. Bacitracin residue concentrations in muscle and monensin residue concentrations in skin with fat were determined.

Results: Bacitracin residue concentrations were less than 0.3 ppm in all the muscle samples. Monensin residue concentrations were less than 0.04 ppm in all the skin/fat samples. The limit of detection was 0.3 ppm for bacitracin in muscle and 0.04 ppm for monensin in skin/fat.

In addition, as described in the FOI Summary for the original approval of NADA 140-937, Study No. AAC8722 also demonstrated noninterference of the analytical method for bacitracin by monensin, and noninterference of the analytical method for monensin by bacitracin.

Conclusions: The residue data from the study supported a zero-day withdrawal period assignment for this approval of the combination of Pennitracin MD® and Coban™ for use in the manufacture of Type C medicated feed for growing turkeys, based on the currently codified tolerances of 0.5 ppm for bacitracin in the edible tissues of turkeys (21 CFR § 556.70). Monensin residue data in the edible tissues of turkey are not needed for withdrawal period determination because a tolerance is not required for monensin residues in the edible tissues of turkeys (21 CFR §556.420).

2. Target Tissues and Marker Residues

   a. Bacitracin

      A target tissue and a marker residue have not been established for bacitracin in turkeys (NADA 141-137, 80 FR 79474, dated December 22, 2015).

   b. Monensin

      A target tissue and a marker residue have not been established for monensin in turkeys (NADA 130-736, 52 FR 15718, dated April 30, 1987).

3. Tolerances

   a. Bacitracin

      The codified tolerance for bacitracin residues in the edible tissues of turkeys is 0.5 ppm (21 CFR § 556.70).

   b. Monensin

      A tolerance for monensin residues in the edible tissues (excluding eggs) of turkeys is not required (21 CFR §556.420).

4. Withdrawal Period

   The results of the tissue residue depletion study (Study No. AAC8722) confirmed a zero-day withdrawal period assignment for the combination of Pennitracin MD® and Coban™ for use in the manufacture of Type C medicated feed for growing turkeys.

D. Analytical Method for Residues

Analytical methods for the individual drugs in this combination are described in NADA 140-937 for combination use of BMD® and Coban™ in turkey feeds (FOI Summary dated November 8, 1994).

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

IV. USER SAFETY

CVM did not require user safety studies for this approval.

V. 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 Pennitracin MD® and Coban™ demonstrate that, when they are used according to the label, they are safe and effective for increased rate of weight gain and improved feed efficiency, and for the prevention of coccidiosis caused by *Eimeria adenoeides*, *E. meleagrimitis* and *E. gallopavonis* in growing turkeys. Additionally, data demonstrate that residues in food products derived from growing turkeys administered Pennitracin MD® and Coban™ will not represent a public health concern when the combination medicated feed is used according to the label.

A. Marketing Status

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the labeling are reasonably certain to be followed in practice.

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.