Date of Approval: December 2, 2022

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-529

Pennitracin MD® and Maxiban™

(bacitracin Type A medicated article) and (narasin and nicarbazin Type A medicated article)

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

Broiler chickens

Supplemental 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 141-529

B. Sponsor

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

Drug Labeler Code: 069254

C. Proprietary Names

Pennitracin MD® and Maxiban™

D. Drug Product Established Names

bacitracin Type A medicated article and narasin and nicarbazin Type A medicated article

E. Pharmacological Categories

Pennitracin MD®: antimicrobial
Maxiban™: 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 of bacitracin (as feed grade bacitracin methylenedisalicylate)
Maxiban™: 36 g/lb of narasin and 36 g/lb of nicarbazin (1:1 ratio)[2]

H. How Supplied

Pennitracin MD®: 50 lb (22.68 kg) bag
Maxiban™: 55.12 lb (25 kg) bag

I. Dispensing Status

Over-the-counter (OTC)

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[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.

[2] Narasin and nicarbazin may only be sourced from Maxiban™, NADA 138-952, which provides these two drugs at a 1:1 ratio.

J. Route of Administration

Oral

K. Species/Class

Broiler chickens

L. Indications and Dosage Regimen

1. For the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens*, and for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* in broiler chickens.

    a. 50 g/ton of bacitracin (as feed grade bacitracin methylenedisalicylate provided by Pennitracin MD®) for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens*

    b. 27 to 45 g/ton each of narasin and nicarbazin (as Maxiban™) for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*

    Feed as the sole ration for 28 to 35 days, starting from the time chicks are placed for brooding.

M. Effect of Supplement

This supplement provides for the new indication, for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens*, and for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* in broiler chickens.

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 narasin and nicarbazin Type A medicated article on the effectiveness and target animal safety of the previously separately approved conditions of use for Pennitracin MD® and Maxiban™ for use in broiler chickens, 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 chickens for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens*	NADA 141-137 (refer to the FOI Summary, dated April 28, 2022)
Maxiban™* Sponsored by Elanco US Inc.	For use in feeds for broiler chickens for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*	NADA 138-952 (refer to the FOI Summary, dated January 18, 1989)

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

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 (as bacitracin methylenedisalicylate),

narasin, and nicarbazin on the human food safety of the previously separately approved conditions of use for Pennitracin MD® and Maxiban™ for use in broiler chickens, 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)
Maxiban™	NADA 138-952 (refer to the FOI Summary, dated July 11, 2018)

C. Residue Chemistry

CVM did not require residue chemistry studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-529 dated September 9, 2020, contains a summary of residue chemistry studies for broiler chickens. The sponsor obtained a right of reference to the data and information in the NADA 140-926 file (FOI Summary, dated January 4, 1999) for combination use of BMD® (bacitracin methylene disalicylate Type A medicated article) and Maxiban™ in chicken feeds to support this approval.

This supplement does not result in any changes to the previously established withdrawal period. The withdrawal period remains zero-day. Refer to the FOI Summary, dated September 9, 2020.

D. Analytical Methods for Residues

The FOI Summary for the original approval of NADA 141-529 dated September 9, 2020, contains the analytical method information for bacitracin, narasin, and nicarbazin in chickens. Analytical methods for the individual drugs in this combination are described in NADA 140-926.

The validated analytical methods for analysis of residues of bacitracin, narasin and nicarbazin in chicken tissues are on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855. To obtain a copy of the analytical method, 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 supplemental 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 Maxiban™ demonstrate that, when they are used according to the label, they are safe and effective for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens*, and for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* in broiler chickens. Additionally, data demonstrate that residues in food products derived from broiler chickens administered Pennitracin MD® and Maxiban™ 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 OTC because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the label are reasonably certain to be followed in practice.

B. Exclusivity

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

C. Supplemental Applications

This supplemental approval did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(2)).

D. Patent Information

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