Date of Approval: October 20, 2023

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-564

Pennchlor® and Rumensin™

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

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

Replacement beef and dairy heifers

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

Sponsored by:

Pharmgate Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 141-564

B. Sponsor

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

Drug Labeler Code: 069254

C. Proprietary Names

Pennchlor® and Rumensin™

D. Drug Product Established Names

chlortetracycline Type A medicated article and monensin Type A medicated article

E. Pharmacological Categories

Pennchlor®: antimicrobial
Rumensin™: anticoccidial

F. Dosage Form

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

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

Pennchlor®: 50, 90 and 100 g/lb of chlortetracycline as chlortetracycline calcium complex equivalent to chlortetracycline hydrochloride
Rumensin™: 90.7 g/lb of monensin, USP

H. How Supplied

Pennchlor®: 22.68 kg (50 lb) bags
Rumensin™: 25 kg (55.12 lb) bags, and 600 kg (1322.77 lb) and 900 kg (1984.16 lb) totes

I. Dispensing Status

Veterinary feed directive (VFD)

J. Route of Administration

[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 B and C medicated feeds that are the subject of this approval.

Oral

K. Species/Classes

Replacement beef and dairy heifers

L. Indications and Dosage Regimens

1. For treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline and for the prevention and control of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii* in replacement beef and dairy heifers.

   a. 400 to 2,000 g/ton of chlortetracycline (as Pennchlor®) for treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline

   b. 15 to 84 g/ton of monensin (as Rumensin™) for the prevention and control of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii*

   For replacement beef and dairy heifers not currently being fed monensin: feed as the sole ration for not more than 5 days to provide 10 mg chlortetracycline per pound of body weight per day and 0.14 to 0.42 mg monensin per pound of body weight per day, depending upon severity of challenge, to provide 50 to 100 mg monensin per head per day in a minimum of 1 pound of Type C feed. After 5 days, continue to feed monensin Type C medicated feed alone to provide 50 to 200 mg monensin per head per day in a minimum of 1 pound of Type C medicated feed.

   For replacement beef and dairy heifers currently being fed monensin: feed as the sole ration for not more than 5 days to provide 10 mg chlortetracycline per pound of body weight per day and 0.14 to 0.42 mg monensin per pound of body weight per day, depending upon severity of challenge, to provide 50 to 200 mg monensin per head per day in a minimum of 1 pound of Type C medicated feed. After 5 days, continue to feed monensin Type C medicated feed alone.

2. For treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline and for increased rate of weight gain in replacement beef and dairy heifers.

   a. 400 to 2,000 g/ton of chlortetracycline (as Pennchlor®) for treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline

   b. 15 to 400 g/ton of monensin (as Rumensin™) for increased rate of weight gain

   For replacement beef and dairy heifers not currently being fed monensin: feed as the sole ration for not more than 5 days to provide 10 mg chlortetracycline per pound of body weight per day and 50 to 100 mg monensin per head per day in a minimum of 1 pound of Type C medicated feed. After 5 days, continue to feed

monensin Type C medicated feed alone to provide 50 to 200 mg monensin per head per day in a minimum of 1 pound of Type C medicated feed.

For replacement beef and dairy heifers currently being fed monensin: feed as the sole ration for not more than 5 days to provide 10 mg chlortetracycline per pound of body weight per day and 50 to 200 mg monensin per head per day in a minimum of 1 pound of Type C feed. After 5 days, continue to feed monensin Type C medicated feed alone.

M. Effect of Supplement

This supplement provides for the addition of replacement beef and dairy heifers with the following indications:

For treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline and for the prevention and control of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii* in replacement beef and dairy heifers; and

For treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to chlortetracycline and for increased rate of weight gain in replacement beef and dairy heifers.

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 chlortetracycline 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 Pennchlor® and Rumensin™ for use in replacement beef and dairy heifers, 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(s)	Approval Information
Pennchlor® Sponsored by Pharmgate Inc.	1. For use in feeds for calves, beef, and non-lactating dairy cattle for treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline.	NADA 138-935 (refer to the FOI Summary, dated February 16, 1996)
Rumensin™* Sponsored by Elanco US Inc.	1. For use in feeds for replacement beef and dairy heifers for increased rate of weight gain. 2. For use in feeds for replacement beef and dairy heifers for the prevention and control of coccidiosis caused by *Eimeria bovis* and *Eimeria zuernii*	NADA 095-735 (refer to 21 CFR 558.355)

* Elanco US Inc. has provided Pharmgate Inc. right of reference to use Rumensin™ 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 chlortetracycline and monensin on the human food safety of the previously separately approved conditions of use for Pennchlor® and Rumensin™ for use in cattle, 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
Pennchlor®	NADA 138-935 (as published in the FEDERAL REGISTER (35 FR 11647) on July 21, 1970, and the FOI Summary, dated February 16, 1996)
Rumensin™	NADA 095-735 (refer to the FOI Summary, dated December 16, 1998)

C. Residue Chemistry

CVM did not require residue chemistry studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-564 dated July 28, 2022, contains a summary of residue chemistry studies for cattle.

This supplement does not result in any changes to the previously established withdrawal period. The withdrawal period remains 0-day. Refer to the FOI Summary, dated July 28, 2022.

D. Analytical Method for Residues

The FOI Summary for the original approval of NADA 141-564 dated July 28, 2022, contains the analytical method summary for chlortetracycline and monensin in cattle.

The validated analytical methods for analysis of residues of chlortetracycline and monensin 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.

The combination labeling contains the following information regarding safety to humans handling, administering, or exposed to the Type B and C medicated feeds:

Keep this and all drugs out of the reach of children. Not for human use.

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 Pennchlor® and Rumensin™ demonstrate that, when they are used according to the label, they are safe and effective for the effect of supplement in the General Information Section above.

Additionally, data demonstrate that residues in food products derived from replacement beef and dairy heifers administered Pennchlor® and Rumensin™ will not represent a public health concern when the combination medicated feed is used according to the label.

A. Marketing Status

A valid 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 veterinary feed directive issued by a licensed veterinarian in the course of their professional practice. In addition, the veterinary feed directives issued for this drug are not refillable.

The decision to restrict this drug to use by or upon a lawful veterinary feed directive issued by a licensed veterinarian was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this drug product, and because restricting this drug product to use by or on the order of a licensed veterinarian is critical for assuring the safe and appropriate use of this drug product in order to mitigate the potential for development of bacterial resistance to antimicrobial drugs.

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 supplement is a Category II supplement as defined in (21 CFR 514.106(b)(2)). This supplemental approval did not require a reevaluation of certain safety or effectiveness data in the application.

D. Patent Information

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