Approval Date: JUL 11, 2001

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-179

Lasalocid sodium (AVATEC®) plus
Bacitracin methylene disalicylate (BMD®)

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

Sponsored by:

Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

FREEDOM OF INFORMATION SUMMARY

Combined use of AVATEC® and BMD® in Growing Turkey Feeds

I. GENERAL INFORMATION:

NADA: 141-179

Sponsor: Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

Generic Names: Lasalocid sodium
Bacitracin methylene disalicylate

Trade Names: AVATEC®
BMD®

Marketing Status: OTC

II. INDICATIONS FOR USE:

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

III. DOSAGE:

A. Dosage form: This NADA provides for the combined use of these two Type A medicated articles: lasalocid sodium as per 21 CFR 558.311, and bacitracin methylene disalicylate as per 21 CFR 558.76(d)(1)(i). Lasalocid sodium is supplied as a Type A medicated article in a concentration of 90.7 grams lasalocid sodium activity per pound. Bacitracin methylene disalicylate is supplied as a Type A medicated article in concentrations of 10, 25, 30, 40, 50, 60, or 75 grams bacitracin activity per pound.

B. Route of Administration: Oral, *via* the feed.

C. Recommended Dosage:

Lasalocid	Lasalocid sodium is added to growing turkey feeds at concentrations from 68 to 113 g/ton for the prevention of coccidiosis caused by

	Eimeria meleagrimitis, E. gallopavonis, and *E. adenoeides.*
Bacitracin methylene disalicylate	Bacitracin methylene disalicylate is added to turkey feeds at concentrations from 4 to 50 g/ton for increased rate of weight gain and improved feed efficiency.

IV. EFFECTIVENESS:

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act of 1996, if the animal drugs/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, FDA will not refuse to approve an NADA for the combination on effectiveness grounds unless the Agency finds that the NADA fails to demonstrate that 1) 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 combination makes a contribution to the labeled effectiveness, 2) 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, or 3) where the combination contains more than one nontopical antibacterial active ingredient/animal drug, there is substantial evidence that each of the nontopical antibacterial active ingredients or animal drugs makes a contribution to the labeled effectiveness.

Lasalocid sodium, as provided by Alpharma Inc., has previously been separately approved for use in growing turkeys for the prevention of coccidiosis caused by *Eimeria meleagrimitis, E. gallopavonis,* and *E. adenoeides* (21 CFR 558.311 (e)(1)(xiv)). Bacitracin methylene disalicylate, as provided by Alpharma Inc., has previously been separately approved for increased rate of weight gain and improved feed efficiency in turkeys (21 CFR 558.76(d)(1)(i)). Effectiveness for each drug, lasalocid sodium and bacitracin methylene disalicylate, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Alpharma Inc.'s approved NADAs 96-298 and 46-592, respectively.

Because lasalocid sodium and bacitracin methylene disalicylate each have at least one use that is different from the other animal drug used in the combination, the NADA must also demonstrate that lasalocid sodium plus bacitracin methylene disalicylate provide appropriate concurrent use for the intended target population. The use of lasalocid sodium plus bacitracin methylene disalicylate provides appropriate concurrent use because these drugs are intended to treat different conditions (lasalocid sodium, coccidiosis; bacitracin methylene disalicylate, performance) likely to occur simultaneously with sufficient frequency in growing turkeys. There is no more than one nontopical antibacterial (bacitracin methylene disalicylate) contained in this combination animal drug intended for use in Type C

medicatedfeed. Lasalocid sodium is not considered to be an antibacterial animal drug for use in growing turkeys for the purposes of §512 (d)(4) of the FFDCA, because lasalocid sodium is approved only for prevention of a protozoal disease in growing turkeys.

V. ANIMAL SAFETY:

In accordance with the FFDCA, as amended by the Animal Drug Availability Act of 1996, if the active ingredients or animal drugs intended for use in combination have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA 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, or a scientific issue is raised by target animal observations contained in studies submitted to the NADA for the combination and FDA finds that the application fails to establish that such a combination active ingredient or animal drug is safe for the target animal.

Lasalocid sodium, as provided by Alpharma Inc., has previously been separately approved for use in turkeys for the prevention of coccidiosis caused by *Eimeria meleagrimitis, E. gallopavonis,* and *E. adenoeides* (21 CFR 558.311 (e)(1)(xiv)). Bacitracin methylene disalicylate, as provided by Alpharma Inc., has previously been separately approved for increased rate of weight gain and improved feed efficiency in turkeys (21 CFR 558.76(d)(1)(i)). Target animal safety for each drug, lasalocid sodium and bacitracin methylene disalicylate, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in approved NADAs 96-298 and 46-592, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of lasalocid sodium or bacitracin methylene disalicylate 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. Thus, pursuant to FFDCA, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety studies are required for approval of NADA 141-179.

VI. HUMAN SAFETY:

In accordance with the FFDCA, as amended by the Animal Drug Availability Act of 1996, if the active ingredients or animal drugs intended for use in combination have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on human safety grounds unless one or more of the active ingredients or animal drugs used in the combination at the longest withdrawal for the respective active ingredients or animal drugs in the combination exceeds the established tolerance, or one or more active ingredients or animal drugs in the combination interferes with the method of analysis for another active ingredient or drug in the combination.

A. Tolerances

Tolerances for residues of bacitracin in uncooked edible tissues of chickens are established at 0.5 ppm (0.02 unit/g) in 21 CFR 556.70. A tolerance of 0.4 ppm for residues of parent lasalocid in turkey liver, the target tissue, is established in 21 CFR 556.347.

B. Residue Data

Residue data supporting the approved individual uses of lasalocid and bacitracin methylene disalicylate, each having zero withdrawal times, were submitted to NADA 96-298 for lasalocid and NADA 46-592 for bacitracin methylene disalicylate.

The tissue residue depletion data and assay non-interference data supporting this combination are found in the FOI summary for the original approval of NADA 141-109. Twenty Nicholas poults (10 males, 10 females) were assigned to one of four treatment groups: unmedicated feed, 125 ppm lasalocid, 55 ppm bacitracin zinc, or 125 ppm lasalocid and 55 ppm bacitracin zinc. The treatment period was from Day 0 to Day 105 of age. On Day 105, after a 6-hour withdrawal period, five birds of each sex were slaughtered from each treatment group. Liver tissue was analyzed for lasalocid. Muscle tissue was analyzed for bacitracin. At zero withdrawal, mean lasalocid residues in the liver were 37.3 $\pm$ 30.4 ppb and mean bacitracin residues were <LOQ of 0.015 ppm for turkeys medicated with feed containing 125 ppm lasalocid and 55 ppm bacitracin zinc. Residues of lasalocid and bacitracin were below their respective tolerances at zero withdrawal. Because their depletion characteristics are very similar, the use of the zinc salt rather than the methylene disalicylate salt of bacitracin is acceptable.

Samples of control liver and control muscle were fortified with lasalocid and bacitracin zinc. The presence of bacitracin zinc did not interfere with the assay of lasalocid in liver and the presence of lasalocid did not interfere with the assay of bacitracin in muscle.

The available residue chemistry information supports the assignment of a zero day withdrawal for growing turkeys fed the combination of lasalocid (68 to 113 g/ton) and bacitracin methylene disalicylate (4 to 50 g/ton).

C. Regulatory Methods for Residues

The method available for measuring lasalocid residues down to 5 ppb in turkey liver is the regulatory HPLC method for lasalocid in chicken skin/fat and in cattle liver, which is described in the FOI summary for NADA 96-298.

A microbiological method is used to assay tissues for bacitracin residues. The method entitled "Modified Microbiological Method for Determination of Bacitracin in Tissues" both methods are on display at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, Maryland 20855.

VII. AGENCY CONCLUSIONS:

The data submitted in support of this NADA comply with the requirements of Section 512 of the FFDCA and demonstrate that lasalocid sodium (68 to 113 g/ton) plus bacitracin methylene disalicylate (4 to 50 g/ton) are safe and effective for the claims indicated in section II of this FOI Summary.

Pursuant to 21 CFR 514.106(b)(2)(vi), this combination NADA approval is regarded as a Category II supplemental change which did not require a reevaluation of safety and efficacy data in the parent NADAs. The drugs are to be fed in Type C medicated feeds, in accordance with section II and III of the FOI Summary and the Blue Bird labeling that is attached to this document.

Attached labeling: Type C Medicated Feed (Blue Bird) – Growing turkeys

Net weight lb (kg) on bag or bulk

Lasalocid sodium/Bacitracin methylene disalicylate Growing Turkey Ration

Type C Medicated Feed

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

Active Drug Ingredient

Lasalocid sodium……..…….……68 to 113 g/ton
Bacitracin methylene disalicylate…….……4 to 50 g/ton

Guaranteed Analysis

Crude Protein, not less than…….…….……_____%
Lysine, not less than……..…….....……_____%
Methionine, not less than……...……...……_____%
Crude Fat, not less than…….……...……_____%
Crude Fiber, not more than……...…….……...……_____%
Calcium, not less than……...…….....……_____%
Calcium, not more than……..……..…….....…_____%
Phosphorus, not less than……..……..…….…_____%
Salt[1], not less than……..…….....……...…_____%
Salt[1], not more than…….…….....……...…_____%
Sodium[2], not less than…….…….....……_____%
Sodium[2], not more than…….…….....……_____%

[1]If added.
[2]Shall be guaranteed only when total sodium exceeds that furnished by the maximum salt guarantee.

Ingredients

Each ingredient must be named in accordance with the names and definitions adopted by the Association of American Feed Control Official's.

Directions for Use

Feed continuously as sole ration.

CAUTION: For growing turkeys only.

MANUFACTURED BY

BLUE BIRD FEED MILL
Anytown, USA 12345