Approval Date: Jan 2, 2001

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-140

Monensin (COBAN®) plus Bacitracin Methylene Disalicylate (BMD®)

1. **As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and for increased rate of weight gain and improved feed efficiency in replacement chickens intended for use as cage layers.**

2. **As an aid in the prevention of coccidiosis caused by by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin in broiler chickens and replacement chickens intended for use as cage layers.**

Sponsored by:

Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

FREEDOM OF INFORMATION SUMMARY

Combined use of COBAN® and BMD® in Broiler Chicken and Replacement Chicken Feeds

I. GENERAL INFORMATION:

NADA: 141-140

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

Generic Names: Monensin
Bacitracin methylene disalicylate

Trade Names: COBAN®
BMD®

Marketing Status: OTC

II. INDICATIONS FOR USE:

As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and for increased rate of weight gain and for improved feed efficiency in replacement chickens intended for use as cage layers;

As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin in broiler chickens and replacement chickens intended for use as cage layers.

III. DOSAGE:

A. Dosage form: This NADA provides for the combined use of these two Type A medicated articles, monensin as per 21 CFR 558.355(f)(1)(i) and (f)(4)(i), and bacitracin methylene disalicylate as per 21 CFR 558.76(d)(1)(i) and (vi). Monensin is supplied as a Type A medicated article in concentrations of 45 or 60 grams monensin activity per pound.

B. 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.

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

D. Recommended Dosage:

Monensin	Monensin is added to broiler chicken and replacement chicken feed at concentrations from 90 to 110 g/ton as an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.
Bacitracin methylene disalicylate	1) Bacitracin methylene disalicylate is added to chicken feed at concentrations from 4 to 50 g/ton for increased rate of weight gain and improved feed efficiency; 2) Bacitracin methylene disalicylate is added to chicken feed at a concentration of 50 g/ton as an aid in the prevention of necrotic enteritis caused by *Clostridium* spp. or other organisms susceptible to bacitracin.

CAUTION: For replacement chickens intended for use as cage layers only. Do not feed to laying chickens. Do not feed to chickens over 16 weeks of age. Do not allow horses, other equines, mature turkeys, or guinea fowl access to feed containing monensin. Ingestion of monensin by horses, mature turkeys, and guinea fowl has been fatal.

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.

Monensin, as provided by Elanco Animal Health, has previously been separately approved for use in broiler chickens and replacement chickens intended for use as cage layers as an aid in the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati*, and *E. maxima* (21 CFR 558.355(f)(1)(i) and (f)(4)(i), respectively). Bacitracin methylene disalicylate, as provided by Alpharma Inc., has previously been separately approved for use in chickens for increased rate of weight gain and improved feed efficiency, and as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin (21 CFR 558.76(d)(1)(i) and (d)(1)(vi), respectively). Effectiveness for each drug, monensin and bacitracin methylene disalicylate, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in approved NADAs 38-878 (to which Alpharma Inc. has a right of reference) and 46-592, respectively.

Because monensin and bacitracin methylene disalicylate each have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that monensin plus bacitracin methylene disalicylate provide appropriate concurrent use for the intended target population. The use of monensin plus bacitracin methylene disalicylate provide appropriate concurrent use because these drugs are intended to treat different conditions (monensin, coccidiosis; bacitracin methylene disalicylate, weight gain, feed efficiency, or necrotic enteritis) likely to occur simultaneously with sufficient frequency in broiler chickens and replacement chickens intended for use as cage layers. There is no more than one nontopical antibacterial (bacitracin methylene disalicylate) contained in this combination animal drug intended for use in Type C medicated feed. Monensin is not considered to be an antibacterial animal drug for such use in chickens for the purposes of Section 512(d)(4) of the FFDCA, because monensin is approved only for prevention of a protozoal disease (coccidiosis) in broiler chickens and replacement chickens.

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.

Monensin, as provided by Elanco Animal Health, has previously been separately approved for use in broiler chickens and replacement chickens intended for use as cage layers as an aid in the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati*, and *E. maxima* (21 CFR 558.355(f)(1)(i) and (f)(4)(i), respectively). Bacitracin methylene disalicylate, as provided by Alpharma Inc., has previously been separately approved for use in chickens for increased rate of weight gain and improved feed efficiency and as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin in broiler chickens and replacement chickens (21 CFR 558.76 (d)(1)(i) and (d)(1)(vi), respectively). Target animal safety for each drug, monensin and bacitracin methylene disalicylate, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in approved NADAs 38-878 (to which Alpharma Inc. has a right of reference) and 46-592, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of monensin 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 141-140.

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

Data establishing the safety of monensin and bacitracin methylene disalicylate (BMD) have been submitted to NADA 38-878, and 46-592, respectively. 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.

B. Residue Data

The combination of 90 to 110 g/ton monensin and 4 to 50 g/ton BMD is already approved for use in broilers with a zero withdrawal period (21 CFR 558.355). The extension of use of the combination to replacement chickens with a zero withdrawal period is acceptable. Additional information on the safety of the combination of monensin and BMD can be obtained through the FOI Summary for NADA 49-463.

C. Regulatory Methods for Residues

The method for monensin is "Determination of Monensin in Tissues and Eggs," Method 5801654, Eli Lilly and Company, Box 708, Greenfield, IN 46140.

A microbiological method is used to assay tissues for bacitracin residues. The method entitled "Modified Microbiological Method for Determination of Bacitracin in Tissues" is on display in the Food and Drug Administration's Freedom of Information Publication Room (Room 1061), 5630 Fisher's Lane, Rockville, MD 20852.

VII. AGENCY CONCLUSIONS:

The data submitted in support of this NADA comply with the requirements of Section 512 of the FFDCA and demonstrate that use of monensin (90 to 110 g/ton) plus bacitracin methylene disalicylate (4 to 50 g/ton and 50 g/ton) with a zero withdrawal period is 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) –Broiler chickens and Replacement chickens intended for use as cage layers.

Net weight lb (kg) on bag or bulk

Monensin/Bacitracin methylene disalicylate Replacement Chicken Ration

Type C Medicated Feed

As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and for increased rate of weight gain and improved feed efficiency in replacement chickens intended for use as cage layers.

Active Drug Ingredient

Monensin……..……..90 to 110 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 Officials.

Directions for Use

Feed continuously as sole ration.

(OVER)

CAUTION: For replacement chickens intended for use as cage layers only. Do not feed to laying chickens. Do not feed to chickens over 16 weeks of age. Do not allow horses, other equines, mature turkeys, or guinea fowl access to feed containing monensin. Ingestion of monensin by horses, mature turkeys, and guinea fowl has been fatal.

MANUFACTURED BY

BLUE BIRD FEED MILL
Anytown, USA 12345

Net weight lb (kg) on bag or bulk

Monensin/Bacitracin methylene disalicylate
Broiler Chicken & Replacement Chicken Ration

Type C Medicated Feed

As an aid in the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*, and as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin in broiler chickens and replacement chickens intended for use as cage layers.

Active Drug Ingredient

Monensin……90 to 110 g/ton
Bacitracin methylene disalicylate ……..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……_____%

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Anytown, USA 12345