

HFA-305
Documents Management Branch

Approval Date APR 29 2002

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 140-865

Narasin (MONTEBAN[®]) plus Bacitracin zinc (ALBAC[®])

**For 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
broiler chickens.**

Sponsored by:

**Alpharma Inc.
One Executive Drive
Fort Lee, New Jersey 07024**

140-865-F01S 2

FREEDOM OF INFORMATION SUMMARY

Combined use of MONTEBAN[®] and ALBAC[®] in Broiler Chicken Feeds

I. GENERAL INFORMATION

NADA: 140-865

Sponsor: Alpha Pharma Inc.
One Executive Drive
Fort Lee, New Jersey 07024

Generic Names: Narasin
Bacitracin zinc

Trade Names: MONTEBAN[®]
ALBAC[®]

Marketing Status: OTC

Effect of Supplement: To provide for the addition of ALBAC[®] (bacitracin zinc) Type A Medicated article as an alternate source of bacitracin zinc for the approved combination of MONTEBAN[®] (narasin) and BACIFERM[®] (bacitracin zinc). No Federal Register required because there is no change to the CFR.

II. INDICATIONS FOR USE

For 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 broiler chickens.

III. DOSAGE

A. Dosage form: This Supplemental NADA provides for the combined use of these two Type A medicated articles: narasin as per 21 CFR 558.363, and bacitracin zinc as per 21 CFR 558.78. Narasin is supplied as a Type A medicated article in concentrations of 36, 45, 54, 72, or 90 grams narasin activity per pound. Bacitracin zinc is supplied as a Type A medicated article in a single concentration of 50 grams of bacitracin zinc activity per pound.

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

C. Recommended Dosage:

Narasin

Narasin is added to broiler chicken feed at concentrations from 54 to 72 g/ton for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima*.

Bacitracin zinc

Bacitracin zinc is added to broiler chicken feed 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 active ingredients or animal drugs 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 demonstrate 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 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 (FFDCA §512 (d)(4)(D)).

Narasin, as provided by Elanco Animal Health, has previously been separately approved for use in broiler chicken feeds for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* (21 CFR 558.363(d)(1)). Bacitracin zinc, as provided by Alpharma Inc., has previously been separately approved for use in broiler chicken feeds for increased rate of weight gain and improved feed efficiency (21 CFR 558.78(d)(1)(i)). Effectiveness for the combination of narasin and bacitracin zinc is contained in the original NADA 140-865 for use of MONTEBAN[®] (narasin) and BACIFERM[®] (bacitracin zinc).

Because narasin and bacitracin zinc each have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that narasin plus bacitracin zinc provide appropriate concurrent use for the intended target population. The use of narasin plus bacitracin zinc provides appropriate concurrent use because these drugs are intended to treat different conditions (narasin, coccidiosis; bacitracin zinc, performance) likely to occur simultaneously with sufficient frequency in broiler chickens. There is no more than one

nontopical antibacterial (bacitracin zinc) contained in this combination animal drug intended for use in Type C medicated feed. Narasin is not considered to be an antibacterial animal drug for use in broiler chickens for the purposes of §512 (d)(4) of the FFDCFA, because narasin is approved only for prevention of a protozoal disease (coccidiosis) in broiler chickens.

V. ANIMAL SAFETY

In accordance with the FFDCFA, as amended by the Animal Drug Availability Act of 1996, if the active ingredients 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 combination active ingredient or animal drug is safe for the target animal.

Narasin, as provided by Elanco Animal Health, has previously been separately approved for use in broiler chicken feeds for the prevention of coccidiosis caused by *Eimeria necatrix*, *E. tenella*, *E. acervulina*, *E. brunetti*, *E. mivati*, and *E. maxima* (21 CFR 558.363(d)(1)). Bacitracin zinc, as provided by Alpharma Inc., has previously been separately approved for use in broiler chicken feeds for increased rate of weight gain and improved feed efficiency (21 CFR 558.78(d)(1)(i)). Target animal safety for the combination of narasin and bacitracin zinc is contained in the original NADA 140-865 for use of MONTEBAN[®] (narasin) and BACIFERM[®] (bacitracin zinc). The Agency has found no substantiated scientific issue relating to the target animal safety of narasin or bacitracin zinc 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 FFDCFA, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety studies are required for approval of NADA 140-865.

VI. HUMAN SAFETY

In accordance with the FFDCFA, 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. Toxicity Studies

Human food safety of this combination product has been established by data in NADA 140-865 for MONTEBAN[®] (narasin) and BACIFERM[®] (bacitracin zinc).

The bioequivalence of ALBAC[®] and BACIFERM[®] for use in broiler chicken feed at concentrations of 4 to 50 g/ton for increased weight gain and improved feed efficiency was established in the approval of ANADA 200-223.

B. Tolerances

The tolerance for bacitracin zinc in the uncooked edible tissues and eggs of chickens is 0.5 ppm (0.02 unit per gram) negligible residue (21 CFR 556.70). A tolerance for narasin residues in chickens is not needed. The safe concentrations for total narasin residues in uncooked chicken tissues are: 0.6 ppm in muscle; 1.8 ppm in liver; 1.2 ppm in skin with adhering fat and fat (21 CFR 556.428).

C. Residue Non-Interference Study

Non-interference among the active ingredients (narasin and bacitracin zinc) in tissue residue depletion at the longest withdrawal time (zero days) or in the performance of the analytical methods for tissue residues was demonstrated in the FOI summary for the original NADA 140-865 (MONTEBAN[®] (narasin) and BACIFERM[®] (bacitracin zinc).

D. Regulatory Methods

The regulatory analytical method for detection of residues of bacitracin zinc is a microbiological test using *Micrococcus luteus* (ATCC 10240) suspension. The method is published by the Food and Drug Administration, "Antibiotic Residues in Milk, Dairy Products and Animal Tissues: Method, Reports, and Protocols, revised October 1968, reprinted December, 1974". A method capable of determining parent narasin in abdominal fat is on file with the Center for Veterinary Medicine. Both methods are available from the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

Narasin plus bacitracin zinc qualifies for a zero withdrawal.

VII. AGENCY CONCLUSIONS

The data submitted in support of this NADA comply with the requirements of §512 of the FFDCA and demonstrate that narasin (54 to 72 g/ton) plus bacitracin zinc (4 to 50 g/ton) are safe and effective for the claims indicated in Section II of this FOI summary.

The marketing status of this supplemental approval is OTC in accordance with the OTC marketing status of the original approval.

Pursuant to 21 CFR 514.106 (b)(2), this supplemental 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

Freedom of Information Summary
NADA 140-865, MONTEBAN[®] + ALBAC[®]
Page 5

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).

Net weight lb (kg) on bag or bulk

Narasin/Bacitracin Zinc (ALBAC[®]) Broiler Chicken Ration Type C Medicated Feed

For 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 broiler chickens.

ACTIVE DRUG INGREDIENT

Narasin.....	54 to 72 g/ton
Bacitracin zinc.....	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.....	%

¹If added.

²Shall 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 the sole ration.

CAUTION: Do not allow adult turkeys, horses or other equines access to formulations containing narasin. Ingestion of narasin by these species has been fatal.

MANUFACTURED BY

BLUE BIRD FEED MILL
Anytown, USA 12345