

JUN 22 1998

**FREEDOM OF INFORMATION SUMMARY**

**NADA 046-592**

**BMD**

**(bacitracin methylene disalicylate)**

**Type A Medicated Article**

“...as an aid in the prevention and control of necrotic enteritis in replacement chickens  
caused or complicated by  
*Clostridium* spp. or other organisms susceptible to bacitracin.”

**SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION**

Sponsored by:

Alpharma Inc.

Date of Approval: \_\_\_\_\_

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**I. GENERAL INFORMATION**

NADA Number: 046-592

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

Generic Name: bacitracin methylene disalicylate

Trade Name: BMD<sup>®</sup>

Marketing Status: OTC

Supplement Effect: This supplement provides for the addition of a class, replacement chickens, to be added to the previously approved product, BMD<sup>®</sup> Type A medicated article.

**II. INDICATIONS FOR USE**

Replacement chickens: as an aid in the prevention and control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin methylene disalicylate.

**III. DOSAGE FORM, ROUTE OF ADMINISTRATION AND RECOMMENDED DOSAGE****A. Dosage Form**

Bacitracin methylene disalicylate is supplied as a Type A medicated article in concentrations of 10, 25, 30, 40, 50, 60, and 75 grams bacitracin activity per pound.

**B. Route of Administration**

Oral, via the feed

**C. Recommended Dosage**

As an aid in the prevention of necrotic enteritis: BMD should be fed to replacement chickens at a concentration of 50 grams per ton of feed.

As an aid in the control of necrotic enteritis: BMD should be fed to replacement chickens at a concentration of 100 to 200 grams per ton of feed for 5 to 7 days or as long as clinical signs persist, and then the concentration should be reduced to prevention level (50 grams/ton).

#### IV. EFFECTIVENESS

Bacitracin methylene disalicylate is approved under this NADA for use in laying chickens, turkeys, pheasants, quail, swine, broiler chickens, growing/finishing swine, pregnant sows, and feedlot beef cattle. Approvals relevant to the present supplement include: bacitracin MD from 10 to 25 grams per ton for use in chickens for increased egg production and improved feed efficiency for egg production [21 CFR 558.76 (d)(1)(iii)]; BMD at 50 grams per ton for use in broiler chickens 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)(vi)]; and BMD from 100 to 200 grams per ton for use in broiler chickens as an aid in the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin [21 CFR 558.76 (d)(1)(ix)]. Since the effectiveness of bacitracin methylene disalicylate for the prevention (50 g/ton) and control (100 to 200 g/ton) of necrotic enteritis in broiler chickens has previously been established under this NADA, and because the agency believes that broiler chickens and replacement chickens are similar enough physiologically that a drug that is effective for this indication in broiler chickens will be equally effective in replacement chickens, additional effectiveness studies were not required for this supplemental application.

#### V. ANIMAL SAFETY

The safety of administering up to 4000 g/ton of BMD in the feed of broiler chickens for up to 8 weeks has previously been demonstrated under this NADA. Similarly, the safety of administering up to 1000 g/ton of BMD in the feed of laying hens for 5 months has also previously been demonstrated under this NADA. For additional information refer to the FOI summaries for the supplemental approvals of bacitracin methylene disalicylate for use in laying chickens for increased egg production and improved feed efficiency for egg production, and for use in broiler chickens as an aid in the prevention and control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin.

Based on the margin of safety previously documented in the safety studies summarized for use of this drug in broiler chickens and laying hens, additional safety studies were not required for this supplemental application.

## VI. HUMAN SAFETY

The human food safety of this product has been previously established under this NADA. For additional information refer to the FOI summaries for the supplemental approvals of bacitracin methylene disalicylate for use in chickens for increased egg production and improved feed efficiency for egg production, for use in broiler chickens as an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin, and for use in broiler chickens as an aid in the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin.

Tolerances for residues of bacitracin from bacitracin methylene disalicylate in the uncooked edible tissue of chickens and turkeys have been established at 0.5 ppm (0.02 unit per gram), negligible residue (21 CFR 556.70).

Earlier FOI Summaries under this NADA highlight two studies in which chickens were fed 1000 g/ton BMD for 8 weeks with no detection of residues in target tissue at zero withdrawal; and laying hens were fed 1000 g/ton for 5 months with no detection of residues either in tissues or egg yolk and egg whites. These two studies are sufficient to support a zero withdrawal period for replacement (breeder and layer) chickens that will be treated with BMD at levels up to 200 g/ton.

A microbiological assay method is used to assay tissues for bacitracin residues. The method entitled "Modified Microbiological Method for Determination of Bacitracin in Tissues" is on file at the Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855.

## VII. AGENCY CONCLUSIONS

The data submitted in support of this NADA supplement satisfy the requirements of Section 512 of the Federal Food, Drug and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that bacitracin methylene disalicylate, when administered in the feed of replacement chickens at a concentration of 50 g/ton (for prevention) or 100 to 200 g/ton (for control), is safe and effective as an aid in the prevention and control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin methylene disalicylate.

The tolerance for residues of bacitracin in edible uncooked tissues of chickens has been established as 0.5 ppm under 21 CFR 556.70. Earlier FOI Summaries under this NADA highlight two studies in which chickens were fed 1000 g/ton BMD for 8 weeks with no detection of residues in target tissue at zero withdrawal; and laying hens were fed 1000 g/ton for 5 months with no detection of residues either in tissues or egg yolk and egg whites. These two studies are sufficient to support a zero withdrawal period for replacement (breeder and layer) chickens that will be treated with BMD at levels up to 200 g/ton.

Proper use by lay persons can be expected because the directions are clearly written and there is reasonable certainty that the conditions of use can and will be followed by the producer. The agency has concluded that this product can be approved for over-the-counter use.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), these are Category II changes. The approval of these changes is not expected to have any adverse effect on the safety or effectiveness of this new animal drug and, therefore, did not require a reevaluation of the human food or target animal safety data in the parent application.

**VIII. APPROVED LABELING**

A copy of the draft facsimile labeling is attached to this document.

- A. BMD<sup>®</sup> 30 Type A Medicated Article Bag Label
- B. BMD<sup>®</sup> 50 Type A Medicated Article Bag Label
- C. BMD<sup>®</sup> 60 Type A Medicated Article Bag Label
- D. BMD<sup>®</sup> Bluebird Label for Type C Medicated Feed (100 to 200 g/ton)
- E. BMD<sup>®</sup> Bluebird Label for Type C Medicated Feed (50 g/ton)

# BMD 30

## BACTRACIN METHYLENE DISALICYLATE TYPE A MEDICATED ARTICLE ANTIBACTERIAL

For Supplementing Rations of Swine,  
Chickens, Turkeys, Pheasants, Quail  
and Feedlot Beef Cattle

### ACTIVE DRUG INGREDIENT

Each pound contains feed grade bacitracin methylene disalicylate equivalent to 30 grams bacitracin (Master Standard).

### COMPOSITION

A dried precipitated fermentation product obtained by culturing *B. brevis* strain Tracy on media adapted for the synthesis of bacitracin methylene disalicylate.

### For Manufacturing Livestock and Poultry Feeds Only

### MIXING DIRECTIONS

Prepare an intermediate premix containing 5 grams per pound by mixing 1.0 lb of BMD 30 with 5.0 lbs of soybean meal or ground corn. Then add 0.8 lb in 50.0 lbs of intermediate premix per ton of finished feed.

	Grams bacitracin per ton of feed	Indications for Use
GROWING/ FINISHING SWINE	10 - 30	For increased rate of weight gain and improved feed efficiency.
	250	For control of swine dysentery (bloody scours) associated with <i>Trichostrongylus axei</i> in pigs up to 250 lbs body weight. Feed 250 grams per ton of complete feed on premises with a history of swine dysentery, but where signs of the disease have not yet occurred or following an approved treatment of the disease condition.  The 250 g ton level will provide 5 to 7 mg/lb in swine weighing 40 to 250 lbs.
PREGNANT SOWS	250	For control of clostridial enteritis caused by <i>C. perfringens</i> in suckling piglets when fed to sows from 14 days before through 21 days after farrowing on premises with a history of clostridial scours.  CAUTION: Diagnosis should be confirmed by a veterinarian when results are not satisfactory. Feed containing an approved level of bacitracin methylene disalicylate should be the sole ration.
BROILER AND REPLACEMENT CHICKENS	4 - 50	For increased rate of weight gain and improved feed efficiency.
	50	As an aid in prevention of necrotic enteritis caused or complicated by <i>Clostridium</i> spp. or other organisms susceptible to bacitracin methylene disalicylate.
	100 - 200	As an aid in control of necrotic enteritis caused or complicated by <i>Clostridium</i> spp. or other organisms susceptible to bacitracin methylene disalicylate.  CAUTION: To control a necrotic enteritis outbreak, start medication at the first clinical signs of disease. The dosage range permitted provides for different levels based on severity of the infection. Consult a poultry diagnostic laboratory or pathologist to determine the diagnosis and advice regarding the optimal level of drug. Administer continuously for 5 - 7 days or as long as clinical signs persist, and then reduce medication to prevention level (50 g/ton).
LAYING HENS	10 - 25	For increased egg production and improved feed efficiency during the first seven months.
GROWING TURKEYS	4 - 50	For increased rate of weight gain and improved feed efficiency.
	200	As an aid in control of transmissible enteritis in growing turkeys complicated by organisms susceptible to bacitracin methylene disalicylate.
PHEASANTS	4 - 50	For increased rate of weight gain and improved feed efficiency.
QUAIL	5 - 20	For increased rate of weight gain and improved feed efficiency in quail not over 5 weeks of age.
	200	For prevention of ulcerative enteritis in growing quail due to <i>Clostridium colinum</i> susceptible to bacitracin methylene disalicylate. Feed continuously as the sole ration.
FEEDLOT BEEF CATTLE	Mg Per Head Per Day 70 (continuously)	For reduction in the number of liver condemnations due to abscesses in feedlot beef cattle.
	250 (3 days in 30)	For reduction in the number of liver condemnations due to abscesses in feedlot beef cattle.

NOTE: Where minimum levels are shown, increase the antibiotic concentration within approved range when necessary to fit the feeding program, and to insure adequate levels of antibiotic in the complete ration.

RESTRICTED DRUG: Use Only as Directed. (CA)  
For Use in Animals Only. For Use in Dry Feeds Only.  
Not for Use in Liquid Feed Supplements.  
NADA 48-592, APPROVED BY FDA

NET WT 50 LB (22.67 kg)

# BMD 30

# BMD 60

## BACITRACIN METHYLENE DISALICYLATE TYPE A MEDICATED ARTICLE ANTIBACTERIAL

For Supplementing Rations of Swine,  
Chickens, Turkeys, Pheasants, Quail  
and Feedlot Beef Cattle

### ACTIVE DRUG INGREDIENT

Each pound contains feed grade bacitracin methylene disalicylate equivalent to 60 grams bacitracin (Master Standard)

### COMPOSITION

A dried precipitated fermentation product obtained by culturing *B. licheniformis* Tracy on media adapted for microbiological production of bacitracin calcium carbonate

### For Manufacturing Livestock and Poultry Feeds Only

### MIXING DIRECTIONS

Prepare an intermediate premix containing 5 grams per pound by mixing 1 0 lb of BMD 60 with 11 0 lbs of soybean meal or ground corn. Then add 0 8 to 50 0 lbs of intermediate premix per ton of finished feed

	Grams bacitracin per ton of feed	Indications for Use
GROWING/ FINISHING SWINE	10 - 30	For increased rate of weight gain and improved feed efficiency
	250	For control of swine dysentery (bloody scours) associated with <i>Treponema hyodysenteriae</i> in pigs up to 250 lbs body weight. Feed 250 grams per ton of complete feed on premises with a history of swine dysentery but where signs of the disease have not yet occurred or following an approved treatment of the disease condition. The 250 g/ton level will provide 5 to 7 mg/lb in swine weighing 40 to 250 lbs
PREGNANT SOWS	250	For control of clostridial enteritis caused by <i>C. perfringens</i> in suckling piglets when fed to sows from 14 days before through 21 days after farrowing on premises with a history of clostridial scours <b>CAUTION:</b> Diagnosis should be confirmed by a veterinarian when results are not satisfactory. Feed containing an approved level of bacitracin methylene disalicylate should be the sole ration
BROILER AND REPLACEMENT CHICKENS	4 - 50	For increased rate of weight gain and improved feed efficiency
	50	As an aid in prevention of necrotic enteritis caused or complicated by <i>Clostridium spp.</i> or other organisms susceptible to bacitracin methylene disalicylate
	100 - 200	As an aid in control of necrotic enteritis caused or complicated by <i>Clostridium spp.</i> or other organisms susceptible to bacitracin methylene disalicylate <b>CAUTION:</b> To control a necrotic enteritis outbreak start medication at the first clinical signs of disease. The dosage range permitted provides for different levels based on severity of the infection. Consult a poultry diagnostic laboratory or pathologist to determine the diagnosis and advice regarding the optimal level of drug. Administer continuously for 5 - 7 days or as long as clinical signs persist, and then reduce medication to prevention level (50 g/ton)
LAYING HENS	10 - 25	For increased egg production and improved feed efficiency during the first seven months of production
GROWING TURKEYS	4 - 50	For increased rate of weight gain and improved feed efficiency
	200	As an aid in control of transmissible enteritis in growing turkeys complicated by organisms susceptible to bacitracin methylene disalicylate
PHEASANTS	4 - 30	For increased rate of weight gain and improved feed efficiency
QUAIL	5 - 20	For increased rate of weight gain and improved feed efficiency in quail not over 5 weeks of age
	200	For prevention of ulcerative enteritis in growing quail due to <i>Clostridium coliform</i> susceptible to bacitracin methylene disalicylate. Feed continuously as the sole ration
FEEDLOT BEEF CATTLE	Mg Per Head Per Day 70 (continuously)	For reduction in the number of liver condemnations due to abscesses in feedlot beef cattle
	250 (5 days in 30)	For reduction in the number of liver condemnations due to abscesses in feedlot beef cattle

NOTE: Where minimum levels are shown, increase the antibiotic concentration within approved range when necessary to fit the feeding program, and to insure adequate levels of antibiotic in the complete ration.

RESTRICTED DRUG: Use only as directed. (CA)

For Use in Animals Only. For Use in Dry Feeds Only.

Not for Use in Liquid Feed Supplements.

NADA 46-582, APPROVED BY FDA

NET WT 50 LB (22.67 kg)

**ALPHARMA INC.**  
One Executive Drive, Fort Lee, New Jersey 07024

APH-015C 9801



# DISALICYLATE TYPE A MEDICATED ARTICLE ANTIBACTERIAL

# 50

For Supplementing Rations of Swine, Chickens, Turkeys, Pheasants, Quail and Feedlot Beef Cattle

## ACTIVE DRUG INGREDIENT

Each pound contains 50 grams bacitracin methylene disacrylate (equivalent to 50 grams bacitracin Molar Standard). A dried precipitated fermentation product obtained by culturing *B. licheniformis* Tracy on media adapted for microbiological production of bacitracin calcium carbonate.

## COMPOSITION

## For Manufacturing Poultry and Livestock Feeds Only

## MIXING DIRECTIONS

Prepare an intermediate premix containing 5 grams per pound by mixing 1 lb of BMD 50 with 9 1/2 lbs of sorghum meal or ground corn. Then add 0.8 to 50 lbs of intermediate premix per ton of finished feed.

Grams bacitracin per ton of feed

Indications for Use

**BROILER AND REPLACEMENT CHICKENS**  
 50 For increased rate of weight gain and improved feed efficiency.  
 100 - 200 As aid in prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin methylene disacrylate.  
 As aid in control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin methylene disacrylate.

**LAYING HENS**  
 10 - 25 For increased egg production and improved feed efficiency; during the first seven months of production.

**GROWING TURKEYS**  
 4 - 50 For increased rate of weight gain and improved feed efficiency.  
 200 As aid in control of transmissible enteritis in growing turkeys complicated by organisms susceptible to bacitracin methylene disacrylate.

**PHASANTS**  
 4 - 50 For increased rate of weight gain and improved feed efficiency.

**QUAIL**  
 5 - 20 For increased rate of weight gain and improved feed efficiency in quail not over 5 weeks of age.  
 200 For prevention of udderitis enteritis in growing quail due to *Escherichia coli* susceptible to bacitracin methylene disacrylate. Feed continuously as the sole ration.

**GROWING/ FINISHING SWINE**  
 10 - 30 For increased rate of weight gain and improved feed efficiency.  
 250 For control of swine dysentery (bloody scours) associated with *Escherichia coli* infections in pigs up to 250 lbs body weight. Feed 250 grams per ton of complete feed on premises with a history of swine dysentery, but where signs of the disease have not yet occurred or following an approved treatment of the disease condition.  
 The 250 gram level will provide 5 to 7 mg/lb in swine weighing 40 to 250 lbs.  
 From 14 days before through 21 days after farrowing on premises with a history of clostridial scours. For control of clostridial enteritis caused by *C. perfringens* in suckling piglets when fed to sows containing an approved level of bacitracin methylene disacrylate should be the sole ration.

**PREGNANT SOWS**  
 250 For reduction in the number of liveborn piglets due to abortions in feedlot beef cattle.  
 (continuously) For reduction in the number of liveborn piglets due to abortions in feedlot beef cattle.  
 (5 days in 30)

**FEEDLOT CATTLE**  
 70 (continuously) For reduction in the number of liveborn calves due to abortions in feedlot beef cattle.  
 (5 days in 30) For reduction in the number of liveborn calves due to abortions in feedlot beef cattle.

NET WT 50 LB (22.67 kg)

NADA 146-592, APPROVED BY FDA  
 Not for Use in Liquid Type B Medicated Feeds.  
 For Use in Animals Only, For Use in Dry Feeds Only.  
 RESTRICTED DRUG - USE ONLY AS DIRECTED. (CAUTION)

NOTE: Where minimum levels are shown, increase the antibiotic concentration within approved range when necessary to fit the feeding program and to insure adequate levels of antibiotic in the complete ration.

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



AHM-0127-1705

Lot No. \_\_\_\_\_

**NET WEIGHT ON BAG OR BULK**

**BLUE BIRD BMD -- CNE  
TYPE C BROILER AND REPLACEMENT CHICKEN FEED  
MEDICATED**

As an aid in the control of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin methylene disalicylate.

**ACTIVE DRUG INGREDIENTS**

Bacitracin methylene disalicylate ..... 100-200 g/ton

**GUARANTEED ANALYSIS**

Crude Protein, not less than ..... %  
Crude Fat, not less than ..... %  
Crude Fiber, not more than ..... %

**INGREDIENTS**

Each ingredient must be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions listed in Title 21 CFR 501.110.

**DIRECTIONS FOR USE**

Feed continuously as the sole ration.

**CAUTION:** To control a necrotic enteritis outbreak, start medication at the first clinical signs of disease. The dosage range permitted provides for different levels based on severity of the infection. Consult a poultry diagnostic laboratory or pathologist to determine the diagnosis and advice regarding the optimal level of drug. Administer continuously for 5-7 days or as long as clinical signs persist, and then reduce medication to prevention level (50 g/ton).

BLUE BIRD FEED MILL  
Any Town, USA 12345

Lot No. \_\_\_\_\_

**NET WEIGHT ON BAG OR BULK**

**BLUE BIRD BMD -- PNE  
TYPE C BROILER AND REPLACEMENT CHICKEN FEED  
MEDICATED**

As an aid in the prevention of necrotic enteritis caused or complicated by *Clostridium* spp. or other organisms susceptible to bacitracin methylene disalicylate.

**ACTIVE DRUG INGREDIENTS**

Bacitracin methylene disalicylate .....50 g/ton

**GUARANTEED ANALYSIS**

Crude Protein, not less than ..... %  
Crude Fat, not less than ..... %  
Crude Fiber, not more than ..... %

**INGREDIENTS**

Each ingredient must be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions listed in Title 21 CFR 501.110.

**DIRECTIONS FOR USE**

Feed continuously as the sole ration.

BLUE BIRD FEED MILL  
Any Town, USA 12345