Date of Approval: October 26, 2016

# FREEDOM OF INFORMATION SUMMARY

## ORIGINAL NEW ANIMAL DRUG APPLICATION

NADA 141-465

INTEPRITY and COBAN

avilamycin and monensin

Type A Medicated Articles to be Used in the Manufacture of Type C Medicated Feeds

Broiler chickens

For the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens;* and as an aid in the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati,* and *E. maxima* in broiler chickens.

Sponsored by:

Elanco US Inc.

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# I. GENERAL INFORMATION

## A. File Number

NADA 141-465

## B. Sponsor

Elanco US Inc.
2500 Innovation Way
Greenfield, IN, 46140

Drug Labeler Code: 058198

## C. Proprietary Name

INTEPRITY and COBAN

## D. Established Name

Avilamycin and monensin

## E. Pharmacological Category

Avilamycin: antimicrobial
Monensin: anticoccidial

## F. Dosage Form

Type A Medicated Articles to be Used in the Manufacture of Type C Medicated Feeds

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

Avilamycin: 45.4 g/lb.
Monensin: 45, 60, 90, or 110 g/lb.

## H. How Supplied

Avilamycin: 55.12 lb. bag
Monensin: 55.12 lb. bag

## I. Dispensing Status

VFD

## J. Dosage Regimen

[1] The sponsors of these individual currently marketed Type A medicated articles may have approvals for other strengths of these products 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 C medicated feeds that is the subject of this approval.

13.6 to 40.9 g avilamycin and 90 to 110 g monensin per ton of Type C medicated feed, to be fed as the sole ration for 21 consecutive days

**K. Route of Administration**

Oral

**L. Species/Class**

Broiler chickens

**M. Indication**

For the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens;* and as an aid in the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati,* and *E. maxima* in broiler chickens.

## II. EFFECTIVENESS

In accordance with the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Animal Drug Availability Act (ADAA) of 1996, if the animal drugs or active ingredients intended for use in combination in an animal feed have already been separately approved for the particular uses and conditions for which they are intended for use in combination, the Center for Veterinary Medicine (CVM) will not refuse to approve an NADA for the combination on effectiveness grounds unless the FDA finds that the sponsor fails to demonstrate that:

- 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.

Avilamycin, as provided by Elanco US Inc., has previously been separately approved for use in feed for broiler chickens for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens* (21 CFR 558.68). Monensin, as provided by Elanco US Inc., has previously been separately approved for use in feed for broiler chickens 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). Effectiveness of each drug, avilamycin and monensin, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Elanco US Inc.'s approved NADAs 141-439 and 038-878 for avilamycin and monensin, respectively.

Because avilamycin and monensin each have at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that avilamycin plus monensin provide appropriate concurrent use for the intended target population. The use avilamycin plus monensin provides appropriate concurrent use because these drugs are intended to treat different conditions (prevention of mortality associated with necrotic enteritis and prevention of coccidiosis, respectively) likely to occur simultaneously with sufficient frequency in broiler chickens. There is no more than one nontopical antibacterial contained in this combination animal drug intended for use in Type C medicated feed.

## III. TARGET ANIMAL SAFETY

In accordance with the FD&C Act, as amended by the ADAA of 1996, if the animal drugs or 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, CVM 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 that cannot adequately be evaluated based on the information contained in the application for the combination, and CVM finds that the application fails to show that the combination is safe, or
- there is a scientific issue raised by target animal observations contained in the studies submitted to the NADA for the combination, and CVM finds that the application fails to show that the combination is safe.

Avilamycin, as provided by Elanco US Inc., has previously been separately approved for use in feed for broiler chickens for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens* (21 CFR 558.68). Monensin, as provided by Elanco US Inc., has previously been separately approved for use in feed for broiler chickens 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).

Under the provisions of ADAA, this original approval allows for the combination of avilamycin (as provided by Elanco US Inc.) and monensin (as provided by Elanco US Inc.). Target animal safety for each drug, avilamycin and monensin, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Elanco US Inc.'s approved NADAs 141-439 and 038-878 for avilamycin and monensin, respectively. The Agency has found no substantiated scientific issue relating to the target animal safety of avilamycin and monensin 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. Therefore, in accordance with the FD&C Act, as amended by the ADAA of 1996, no specific target animal safety studies are required for approval of this application.

## IV. HUMAN FOOD SAFETY

In accordance with the FD&C Act, as amended by the ADAA of 1996, if the animal drugs or active ingredients intended for use in combination in animal feed have already been separately approved for the particular uses and conditions of use for

which they are intended for use in combination, CVM will not refuse to approve an NADA for the combination on human food safety grounds unless CVM finds that the application fails to establish that:

- 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, or
- 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. Toxicology

Safety of the individual drugs in this combination drug have been established by data in NADA 141-438 for avilamycin (FOI Summary dated May 8, 2015), and NADA 038-878 (35 FR 7734, dated May 20, 1970) and NADA 095-735 (40 FR 58289, dated December 16, 1975) for monensin.

## B. Residue Chemistry

1. Summary of Residue Chemistry Studies

   CVM did not require residue chemistry studies for this approval. Data demonstrating residue depletion and assay noninterference for avilamycin and monensin were not required because neither a target tissue nor a marker residue is codified for avilamycin or monensin in chickens and neither compound requires a tolerance in chickens.

2. Target Tissue and Marker Residue Assignment

   No reassessments of target tissue and marker residue were needed for this approval. Neither a target tissue nor a marker residue is codified for avilamycin or monensin in chickens.

3. Tolerance Assignments

   A tolerance for residues of avilamycin in chickens is not required (21 CFR 556.68). A tolerance for residues of monensin in chickens is not required (21 CFR 556.420).

4. Withdrawal Time

   Based on the data summarized in NADA 141-439 and NADA 038-878 for avilamycin and monensin, respectively, a 0-day withdrawal is assigned for chickens fed avilamycin at 40.9 g/ton of feed and monensin at 110 g/ton of feed for up to 21 days.

## C. Microbial Food Safety

With respect to the human food safety evaluation for these types of combination new animal drug approvals, the agency is permitted only to evaluate 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 N-

141465-A-0000-OT 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 Federal Food, Drug, and Cosmetic Act). Therefore, we did not 1) assess the impact of this combination of avilamycin and monensin on antimicrobial resistance among bacteria of public health concern in or on treated chickens, or 2) assess the impact of residues of avilamycin and monensin in edible food products from treated chickens on human intestinal flora, or 3) need to establish a microbiological acceptable daily intake.

### D. Analytical Method for Residues

Because a tolerance has not been assigned for avilamycin or monensin, validated analytical methods are not necessary.

## V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to the Type C medicated feed:

Not for use in humans. Keep out of reach of children.

## VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR part 514. The data contained in the previously approved NADAs for INTEPRITY and COBAN demonstrate that, when they are used according to the label, they are safe and effective for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens;* and as an aid in the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati,* and *E. maxima* in broiler chickens. Additionally, data demonstrate that residues in food products derived from broiler chickens treated with INTEPRITY and COBAN will not represent a public health concern when the product is used according to the label.

### A. Marketing Status

A valid veterinary feed directive (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 VFDs issued for this drug are not refillable.

Labeling restricts this drug to use under the professional supervision of a licensed veterinarian. The decision to restrict this drug to use by or upon a lawful VFD issued by a licensed veterinarian was based on the following factors: (a) adequate directions cannot be written to enable lay persons to appropriately and safely use this product and (b) restricting this drug to use by or upon a lawful VFD issued by a licensed veterinarian should help prevent indiscriminate use, which could result in violative tissue residues.

## B. Exclusivity

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

## C. Patent Information

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