FREEDOM OF INFORMATION SUMMARY

NADA 104-646

Monensin Sodium (Rumensin®) plus Tylosin Phosphate (Tylan®)

Sponsored by :

Elanco Animal Health

Lilly Corporate Center

Indianapolis, Indiana 46285

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I. GENERAL INFORMATION

NADA Number: 104-646

Sponsor: Elanco Animal Health
Lilly Corporate Center
Indianapolis, Indiana 46285

Accepted Name: Rumensin® (monensin sodium), and Tylan® (tylosin phosphate)

Marketing Status: OTC

Effect of the Supplement:

21 CFR 558.355 currently provides for the combination use of monensin and tylosin at 5 to 30 g monensin/ton of medicated feed and 8 to 10 g tylosin/ton of medicated feed to provide 50 to 360 mg monensin/head/day and 60 to 90 mg tylosin/head/day in cattle fed in confinement for slaughter for improved feed efficiency and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes*.

This supplement provides for the treatment of the approved combination of monensin plus tylosin to be treated as a combination under the provisions of the Animal Drug Availability Act of 1996, and its reference to feed delivered drug combinations. The effect is to provide for the addition of the coccidiosis claim to this combination (monensin, 10-30 g/ton of medicated feed to provide 0.14 to 0.42 mg/lb body weight, depending on the severity of the challenge, up to 360 mg/head/day; tylosin 8-10 g/ton of medicated feed to provide 60-90 mg/head/day) in Type B and C medicated feeds for cattle fed in confinement for slaughter for improved feed efficiency; prevention and control of coccidosis due to *Eimeria bovis* and *E. zuernii*; and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes.*

II. INDICATIONS FOR USE

For improved feed efficiency, the prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*, and the reduction of the incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces (Corynebacterium) pyogenes* in cattle being fed in confinement for slaughter.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE

A. Dosage Form

Rumensin® is supplied as a Type A medicated article at the concentrations of 80 grams of monensin activity per pound of premix. Tylan® is supplied as a Type A mediated article at the concentrations of 40 and 100 grams of tylosin activity per pound of premix. Monensin and tylosin may also be combined in a liquid Type B Medicated feed.

B. Route of Administration

Oral, via the feed

C. Recommended Dosage

Cattle fed in confinement for slaughter should receive 10 to 30 g monensin/ton and 8 to 10 g tylosin/ton in complete feed to provide 0.14 to 0.42 mg monensin/lb body weight, depending on the severity of the challenge, up to 360 mg/head/day monensin and 60 to 90 mg tylosin/head/day.

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 feeds 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 evidence to demonstrate that 1) any active ingredient or animal drug in 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 the other active ingredients or animal drugs used in 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 animals drugs makes a contribution to the labeled effectiveness [FFDCA 512(d)(4)(D)].

Monensin, as provided by Elanco, has previously been separately approved at 10-30 g/ton for improved feed efficiency and prevention and control of coccidosis due to *Emeria bovis* and *E. zuernii* (21 CFR 558.355 (f)(3)(vii)). Tylosin, as provided by Elanco, has previously been separately approved at 8-10 g/ton for use in feed for beef cattle for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces (Corynebacterium) pyogenes* (21 CFR 558.625 (f)(1)(i)). Under the provisions of ADAA, this supplement allows for the addition of the monensin coccidiosis claim and approved separately for use in cattle for the prevention of coccidiosis to provide 0.14 to 0.42 mg/lb body weight, depending on the severity of the challenge, up to 360 mg/head/day. Effectiveness for monensin and tylosin when administered alone in accordance with their approved uses and conditions of use, are demonstrated in Elanco Animal Health's NADA 95-735 and 12-491.

Monensin is intended for a different use than tylosin and therefore the NADA need not demonstrate, by substantial evidence, that monensin contributes to the labeled effectiveness of the combination. Monensin with tylosin provide appropriate concurrent use because these drugs are intended to treat different conditions (monensin, improved feed efficiency and coccidosis; and tylosin, liver abscesses) likely to occur simultaneously with sufficient frequency in cattle fed in confinement for slaughter. There is no more than one nontopical antibacterial contained in this combination animal drug intended for use in Type B and C medicated feeds. Monensin is not considered to be an antibacterial animal drug for use in cattle fed in confinement for slaughter for the purposes of 512(d)(4) of the FFDCA, because monensin is classified as an ionophore.

V. ANIMAL SAFETY

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 feeds 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 substantial scientific issues specific to an active ingredient or animal drug used in the combination or a scientific issue raised by target animal observations contained in studies submitted to the NADA for the combination and the FDA finds that the application fails to establish that such combination of active ingredients or animal drugs is safe for the target animal.

Monensin, as provided by Elanco, has previously been separately approved at 10-30 g/ton for improved feed efficiency and prevention and control of coccidosis due to *Emeria bovis* and *E. zuernii* (21 CFR 558.355 (f)(3)(vii)). Tylosin, as provided by Elanco, has previously been separately approved 8-10 g/ton for use in feed for beef cattle for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces (Corynebacterium) pyogenes* (21 CFR 558.625 (f)(1)(i)). Under the provisions of ADAA, this supplement allows for the addition of the monensin coccidiosis claim, as provided by Elanco Animal Health, and approved separately for use in cattle for the prevention and control of coccidiosis due to *Emeria bovis* and *E. zuernii* to provide 0.14 to 0.42 mg/lb body weight, depending on the severity of the challenge, up to 360 mg/head/day. Target animal safety for each drug, monensin and tylosin, when administered alone in accordance with its approved uses and conditions of use, are demonstrated in Elanco Animal Health's NADA 95-735 and 12-491, respectively.

The Agency has not found any substantial scientific issues relating to the target animal safety of monensin, or tylosin when used in combination under this NADA and no scientific issues has been raised by target animal observations submitted as a part of this NADA for this combination. Thus, pursuant to FFDCA, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety study(ies) are required for this supplemental approval of NADA 104-646.

VI. HUMAN SAFETY

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 of animal drugs intended for use in combination have 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 time for the respective active ingredients or animal drugs exceeds the established tolerances, or one or more of the active ingredients or animal drugs in the combination interferes with the method of analysis for another active ingredient or animal drug in the combination. Safety of this combination product has been established by data in NADA 12-491 for tylosin, and NADA 95-735 for monensin.

For monensin, a tolerance of 0.05 ppm is established for negligible residue of monensin in the edible tissues of cattle and goats as codified under 21 CFR 556.420.

For tylosin, a tolerance of 0.2 ppm is established for negligible residue of tylosin in uncooked fat, muscle, liver, and kidney in cattle as codified under 21 CFR 556.740.

Please refer to the FOI for the original approval for NADA 104-646 dated March 6, 1976 for additional human safety information concerning the use of monensin plus tylosin in cattle fed in confinement for slaughter.

B. Withdrawal Time

There is a 0 day withdrawal for Tylan® and Rumensin®. Refer to the approved NADAs (NADA 12-491, and 95-735, respectively). Tissue residue non-interference was adequately shown, therefore the combination qualifies for a zero withdrawal period.

E. Regulatory Method

The approved regulatory methods for tylosin and monensin may be found in the approved NADAs(NADA 12-491, and 95-735, respectively).

F. User Safety Concern

Refer to the MSDS's for tylosin and monensin (NADAs 12-491, and 95-735, respectively) by contacting the manufacturer for the MSDS.

VII. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA complies with the requirements of Section 512 of the FFDCA and demonstrate that monensin (10 to 30 g/ton of medicated feed to provide 50 to 360 mg/head/day) plus tylosin (8 to 10 g/ton of medicated feed to provide 60 to 90 mg/head/day) is safe and effective for improved feed efficiency; prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*; and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes.*

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. This action did require a reevaluation of the safety and effectiveness data in the parent application.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food producing animals does not qualify for marketing exclusivity because the supplemental application does not contain substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval and conducted or sponsored by the applicant.

VIII. ATTACHED LABELING

A. Type B Bluebird Label For Rumensin® and Tylan®

B. Type B Liquid Bluebird label for RUMENSIN® and TYLAN®

C. TYPE C BLUEBIRD LABEL FOR RUMENSIN® AND TYLAN®