Date of Approval: March 13, 2012

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-473

TYLOVET Soluble
(tylosin tartrate)

Soluble Powder

Chickens, Turkeys, Swine, and Honey Bees

The effect of the supplement is to add new indications to the product labeling for swine to include: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by tylosin phosphate Type A medicated article in feed, and for the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by tylosin phosphate Type A medicated article in feed.

Sponsored by:

Huvepharma AD

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I. GENERAL INFORMATION:

A. File Number: ANADA 200-473

B. Sponsor:

Huvepharma AD
33, James Boucher Blvd., Sophia 1407
Bulgaria

Drug Labeler Code: 016592

U.S. Agent:
Kelly W. Beers, Ph.D.
Huvepharma Inc.
525 Westpark Drive, Suite 230
Peachtree City, GA 30269

C. Proprietary Name: TYLOVET Soluble

D. Established Name: Tylosin tartrate

E. Pharmacological Category: Antimicrobial

F. Dosage Form: Powder

G. Amount of Active Ingredient: 100 g tylosin tartrate per pouch and per jar

H. How Supplied: 100 g pouch, 100 g jar

I. How Dispensed: OTC

J. Dosages:

Chickens: 2 g tylosin per gallon of water for 1 to 5 days depending on the severity of infection. Treated chickens must consume enough medicated drinking water to provide 50 mg per pound of body weight per day. Only medicated water should be available to the birds.

Turkeys: 2 g tylosin per gallon of water for 2 to 5 days depending on the severity of infection. Treated turkeys must consume enough medicated drinking water to provide 60 mg per pound of body weight per day. Only medicated water should be available to the birds.

Swine: 250 mg tylosin per gallon of water for 3 to 10 days, depending on the severity of infection. Only medicated water should be available.

Honey bees: Mix 200 mg tylosin in 20 g confectioners/powdered sugar. Use immediately. Apply (dust) this mixture over the top bars of the brood chamber once weekly for 3 weeks.

K. Route of Administration: Oral in water or sugar

L. Species/Class: Chickens, turkeys, swine, and honey bees.

M. Indications:

Chickens: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin at time of vaccination or other stress in chickens. For the control of chronic respiratory disease (CRD) associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens.

Turkeys: For maintaining weight gain and feed efficiency in the presence of infectious sinusitis associated with *Mycoplasma gallisepticum* sensitive to tylosin.

Swine: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae.* For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by tylosin phosphate Type A medicated article in feed. For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by tylosin phosphate Type A medicated article in feed.

Honey Bees: For the control of American Foulbrood (*Paenibaccillus larvae*).

N. Reference listed new animal drug: TYLAN Soluble; tylosin tartrate; NADA 013-076; Elanco Animal Health, A Division of Eli Lilly & Co.

O. Effect of Supplement: This supplement provides for changes in the labeled indications to include: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by tylosin phosphate Type A medicated article in feed, and for the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by tylosin phosphate Type A medicated article in feed.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Paten Term Restoration Act of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the reference listed new animal drug (RLNAD), which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Huvepharma AD was granted a waiver from the requirement for an *in vivo* bioequivalence study for TYLOVET Soluble powder formally PHARMASIN Soluble powder. The generic product is administered orally in water or sugar, contains the same active ingredient in the same concentration and dosage form as the RLNAD product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient.

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this supplemental approval.

IV. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this supplemental approval.

V. HUMAN FOOD SAFETY:

- **Tolerances for Residues**:
  The tolerance established for the pioneer product applies to the generic product. A tolerance of 0.2 part per million (ppm) (negligible residue) is established for tylosin residues in eggs and the uncooked edible tissues in uncooked fat, muscle, liver and kidney of chickens, turkeys and swine under 21 CFR 556.740.

- **Withdrawal Times:**
  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.
  A withdrawal periods have been established for the indicated species: 24 hours for chickens, 5 days for turkeys, 48 hours in swine and 4 weeks before main honey flow in honey bees (21 CFR 520.2640).

- **Regulatory Method for Residues:**
  The analytical method for the determination of tylosin in honey is a microbiological assay using an oxytetracycline-resistant strain of *Paenibacillus larvae* in tissues (the causative agent of American foulbrood disease of honey bees). A copy of the method is on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

  The analytical method for the determination of tylosin residues in tissues uses a microbiological assay procedure. This method is found in the Food Additives Analytical Manual on file at the Center for Veterinary Medicine, FDA, 7500 Standish Place, Rockville, MD 20855.

VI. USER SAFETY:

CVM did not require user safety studies for this supplemental approval.

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to TYLOVET Soluble:

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

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that TYLOVET Soluble when used according to the label, is safe and effective.