Date of Approval: May 21, 2014

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-530

PAYLEAN plus TYLOVET 100

ractopamine hydrochloride plus tylosin phosphate

Type A Medicated Articles For Use in the Manufacture of Type B and C Medicated Feeds

Finishing Swine

For increased rate of weight gain, improved feed efficiency and increased carcass leanness in finishing swine, weighing not less than 150 lbs fed a complete ration containing at least 16% crude protein for the last 45 to 90 lbs of gain prior to slaughter; for treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*; and for control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis*.

Sponsored by:

Huvepharma AD

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I. GENERAL INFORMATION:

A. File Number

ANADA 200-530

B. Sponsor

Huvepharma AD
5th Floor, 3A Nikolay Haitov Str.
1113 Sofia, Bulgaria

Drug Labeler Code: 016592

Representative Name and Address: Kelly W. Beers, Ph.D.
Huvepharma, Inc.
525 Westpark Drive, Suite 230
Peachtree City, GA 30269

C. Proprietary Name

PAYLEAN plus TYLOVET 100

D. Established Name

ractopamine hydrochloride plus tylosin phosphate

E. Pharmacological Category

Ractopamine hydrochloride – beta-adrenergic agonist
Tylosin phosphate – antimicrobial

F. Dosage Form

Type A medicated articles for use in the manufacture of dry Type B and C medicated feeds

G. Amount of Active Ingredient in Currently Marketed Products*

Ractopamine hydrochloride – 9 to 45.4 g/lb
Tylosin phosphate –100 g/lb

*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 the Type C medicated feed that is the subject of this approval.

H. How Supplied

PAYLEAN 9 and 45 (ractopamine hydrochloride) – 25 lb bag
TYLOVET 100 (tylosin phosphate) – 50 lb bag

I. Dispensing Status

OTC

J. Dosage Regimen

Ractopamine hydrochloride is added to finishing feed at concentrations of 4.5 to 9 g/ton for increased rate of weight gain, improved feed efficiency and increased carcass leanness in finishing swine, weighing not less than 150 lbs, fed a complete ration containing at least 16% crude protein for the last 45 to 90 lbs of gain prior to slaughter. No increased benefit has been shown when ractopamine concentrations in the diet are greater than 4.5 g/ton.

Tylosin phosphate is added to swine feed at concentrations of 40 to 100 g/ton of complete feed for 2 to 6 weeks immediately after medicating with 250 mg tylosin tartrate per gallon in drinking water for 3 to 10 days for treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* and for control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis*.

Tylosin phosphate is added to swine feed at concentrations of 100 g/ton for at least 3 weeks followed by 40 g/ton until market weight for control of swine dysentery associated with *Brachyspira hyodysenteriae* and for control of porcine proliferative enteropathies (ileitis) associated with *Lawsonia intracellularis*.

Tylosin phosphate is added to swine feed at concentrations of 100 g/ton for 21 days for control of porcine proliferative enteropathies (ileitis) associated with *Lawsonia intracellularis*.

K. Route of Administration

Oral, in feed

L. Species/Class

Finishing swine

M. Indications

Ractopamine hydrochloride 4.5 to 9.0 g/ton and tylosin phosphate 40 to 100 g/ton for 2 to 6 weeks immediately after medicating with 250 mg tylosin tartrate (as TYLAN Soluble) per gallon in drinking water for 3 to 10 days: For increased rate of weight gain, improved feed efficiency and increased carcass leanness in finishing swine, weighing not less than 150 lbs, fed a complete ration containing at least 16% crude protein for the last 45 to 90 lbs of gain prior to slaughter; for treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*; and for control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis*.

Ractopamine hydrochloride 4.5 to 9.0 g/ton and tylosin phosphate 100 g/ton for at least 3 weeks followed by 40 g/ton until market weight: For increased rate of weight gain, improved feed efficiency and increased carcass leanness in finishing swine, weighing not less than 150 lbs, fed a complete ration containing at least

16% crude protein for the last 45 to 90 lbs of gain prior to slaughter; for control of swine dysentery associated with *Brachyspira hyodysenteriae*; and for control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis*.

Ractopamine hydrochloride 4.5 to 9.0 g/ton and tylosin phosphate 100 g/ton: For increased rate of weight gain, improved feed efficiency and increased carcass leanness in finishing swine, weighing not less than 150 lbs, fed a complete ration containing at least 16% crude protein for the last 45 to 90 lbs of gain prior to slaughter; and for control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis*.

N. Approved Original Generic Type A Medicated Article

TYLOVET 100; tylosin phosphate; ANADA 200-484; Huvepharma AD

O. Reference Listed New Animal Drug

PAYLEAN plus TYLAN 100; ractopamine hydrochloride plus tylosin phosphate; NADA 141-172; Elanco Animal Health, A Division of Eli Lilly & Co.

The individual Type A medicated articles approved for use in the manufacture of combination medicated feeds:
PAYLEAN; ractopamine hydrochloride; NADA 140-863; Elanco Animal Health, A Division of Eli Lilly & Co.
TYLAN 100; tylosin phosphate; NADA 012-491; Elanco Animal Health, A Division of Eli Lilly & Co.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent 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.

According to CVM's fourth policy letter issued on November 2, 1989, with regard to the implementation of GADPTRA, after the approval of an ANADA for a generic Type A medicated article, the generic sponsor is entitled to approval for all the feed-mixed combinations for which the RLNAD is approved. Bioequivalence and tissue residue studies are not required for the approval of the generic feed use combinations (Type B or C medicated feeds). Ractopamine hydrochloride is codified under 21 CFR 558.500 and tylosin phosphate is codified under 21 CFR 558.625. The combination of ractopamine hydrochloride and tylosin phosphate is codified under 21 CFR 558.500.

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this approval.

IV. TARGET ANIMAL SAFETY:

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

V. HUMAN FOOD SAFETY:

The following are assigned to this product for finishing swine:

A. Tolerances for Residues:

The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product.

A tolerance of 0.2 part per million (ppm) (negligible residue) is established for residues of tylosin in uncooked fat, muscle, liver, and kidney of swine under 21 CFR 556.740.

A tolerance of 0.15 part per million is established for residues of ractopamine in swine liver (target tissue) and 0.05 ppm (marker residue) in muscle of swine under 21 CFR 556.570.

B. Withdrawal Periods:

Because a waiver from the requirement to demonstrate bioequivalence was granted for the Type A medicated article TYLOVET 100, the withdrawal times for the combination Type B and C medicated feeds are those previously assigned to the RLNAD.

Ractopamine hydrochloride and tylosin phosphate in combination are approved with a zero withdrawal period in finishing swine.

C. Regulatory Method for Residues:

The determination of residues of ractopamine in the liver and muscle of swine is by High Performance Liquid Chromatography (HPLC). The confirmation of residues of ractopamine in the liver and muscle of swine is by Liquid Chromatography/Electrospray Ionization Triple Tandem Quadrupole Mass Spectrometry (LC/ESI-MS-MS). The validated regulatory methods for determination and confirmation of residues of ractopamine are available from CVM, FDA, 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 approval.

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

WARNING
The active ingredient, ractopamine hydrochloride, is a beta-adrenergic agonist. Individuals with cardiovascular disease should exercise special caution to avoid

exposure. Not for use in humans. Keep out of the reach of children. The ractopamine hydrochloride formulation (Type A Medicated Article) poses a low dust potential under usual conditions of handling and mixing. When mixing and handling ractopamine hydrochloride, use protective clothing, impervious gloves, protective eye wear, and a NIOSH-approved dust mask. Operators should wash thoroughly with soap and water after handling. If accidental eye contact occurs, immediately rinse eyes thoroughly with water. If irritation persists, seek medical attention. The material safety data sheet contains more detailed occupational safety information. To report adverse effects, access medical information, or obtain additional product information, contact your ractopamine supplier.

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 PAYLEAN plus TYLOVET 100, when used according to the label, is safe and effective.