Date of Approval: September 20, 2019

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-644

Optaflexx™ and Monovet® and Tylovet®

(ractopamine hydrochloride Type A medicated article) and (monensin Type A medicated article) and (tylosin phosphate)

Type A medicated articles to be used in the manufacture of Type B and Type C medicated feeds

Cattle fed in confinement for slaughter

Original abbreviated new animal drug approval of a medicated feed combination for the indications listed in Section I.L

Sponsored by:

Huvepharma EOOD

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I. GENERAL INFORMATION

A. File Number

ANADA 200-644

B. Sponsor

Huvepharma EOOD,
5th Floor, 3A Nikolay Haytov Str.,
1113 Sofia, Bulgaria

Drug Labeler Code: 016592

US Agent Name and Address:
Kelly Beers, Ph.D.
Huvepharma, Inc.
525 West Park Drive
Peachtree City, GA 30269

C. Proprietary Name

Optaflexx™ and Monovet® and Tylovet®

D. Drug Product Established Name

ractopamine hydrochloride Type A medicated article and monensin Type A medicated article and tylosin phosphate

E. Pharmacological Categories

Optaflexx™: Beta adrenergic agonist
Monovet®: Ionophore, anticoccidial
Tylovet®: Antimicrobial

F. Dosage Form

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

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

Optaflexx™: 45.4 g/lb (100 g/kg) of ractopamine hydrochloride
Monovet®: 90.7 g/lb of monensin
Tylovet®: 40 g/lb and 100 g/lb of tylosin

[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 B and Type C medicated feeds that are the subject of this approval.

H. How Supplied

Optaflexx™ (ractopamine hydrochloride Type A medicated article): 25 lb (11.34 kg) bags
Monovet® (monensin Type A medicated article): 55.12 lb (25 kg) bags
Tylovet® (tylosin phosphate): 50 lb (22.68 kg) bags

I. Dispensing Status

VFD

J. Route of Administration

Oral

K. Species/Class

Cattle fed in confinement for slaughter

L. Indications and Dosage Regimens

1. For increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

    a. Not to exceed 800 g/ton Optaflexx™ for increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

    Feed a minimum of 1.0 lb/hd/day Ractopamine Type C Top Dress TD + MT continuously to cattle fed in confinement for slaughter, to provide 70 to 400 mg/head/day ractopamine for the last 28 to 42 days on feed. Feed on top of a ration containing 10 to 40 g/ton monensin and 8 to 10 g/ton tylosin phosphate, to provide 0.14 to 0.42 mg monensin/lb body weight/day, depending on the severity of the coccidiosis challenge, up to 480 mg/hd/day and 60 to 90 mg/hd/day tylosin.

    Increased benefit for improved feed efficiency, when Optaflexx™ and Monovet® are used together vs. individually cannot be assumed because demonstration of increased effectiveness was not required for approval of this generic combination or the RLNAD combination, NADA 141-224.

2. For increased rate of weight gain, improved feed efficiency, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* and reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and

Arcanobacterium (Actinomyces) pyogenes in cattle fed in confinement for slaughter for the last 28 to 42 days on feed.

a. 8.2 to 24.6 g/ton of Optaflexx™ for increased rate of weight gain and improved feed efficiency in cattle fed in confinement for slaughter for the last 28 to 42 days on feed.

b. 10 to 40 g/ton of Monovet® for improved feed efficiency and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter.

c. 8 to 10 g/ton of Tylovet® for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Arcanobacterium (Actinomyces) pyogenes*.

Feed continuously as sole ration to provide 70 to 430 mg/hd/day ractopamine and 0.14 to 0.42 mg monensin/lb body weight per day, depending on the severity of the coccidiosis challenge, up to 480 mg/hd/day and 60 to 90 mg/hd/day tylosin for the last 28 to 42 days on feed.

Increased benefit for improved feed efficiency, when Optaflexx™ and Monovet® are used together vs. individually cannot be assumed because demonstration of increased effectiveness was not required for approval of this generic combination or the RLNAD combination, NADA 141-224.

3. For increased rate of weight gain, improved feed efficiency, increased carcass leanness, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* and reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Arcanobacterium (Actinomyces) pyogenes* in cattle fed in confinement for slaughter for the last 28 to 42 days on feed.

   a. 9.8 to 24.6 g/ton Optaflexx™ for increased rate of weight gain, improved feed efficiency and increased carcass leanness in cattle fed in confinement for slaughter for the last 28 to 42 days on feed.

   b. 10 to 40 g/ton Monovet® for improved feed efficiency and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter.

   c. 8 to 10 g/ton Tylovet® for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Arcanobacterium (Actinomyces) pyogenes*.

   Feed continuously as sole ration to provide 90 to 430 mg/hd/day ractopamine and 0.14 to 0.42 mg monensin/lb body weight per day, depending on the severity of the coccidiosis challenge, up to 480 mg/hd/day and 60 to 90 mg/hd/day tylosin for the last 28 to 42 days on feed.

   Increased benefit for improved feed efficiency, when Optaflexx™ and Monovet® are used together vs. individually cannot be assumed because demonstration of increased effectiveness was not required for approval of this generic combination or the RLNAD combination, NADA 141-224.

M. Reference Listed New Animal Drug Combination

Optaflexx™ (ractopamine hydrochloride Type A medicated article) and Rumensin™ (monensin Type A medicated article) and Tylan™ (tylosin phosphate); NADA 141-224; Elanco US Inc.

N. Approved Original Generic Type A Medicated Article

Monovet®; monensin Type A medicated article; ANADA 200-639; Huvepharma EOOD

O. Individual Type A medicated articles approved for use in the manufacture of the Type B and Type C combination medicated feeds in this application

Optaflexx™ (ractopamine hydrochloride Type A medicated article); NADA 141-221; Elanco US Inc.
Monovet® (monensin Type A medicated article); ANADA 200-639; Huvepharma EOOD
Tylovet® (tylosin phosphate); ANADA 200-484; Huvepharma EOOD

II. BIOEQUIVALENCE

Under the provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) 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, monensin is codified under 21 CFR 558.355, tylosin is codified under 21 CFR 558.625. The combination of ractopamine hydrochloride, monensin and tylosin is codified under 21 CFR 558.625.

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 cattle fed in confinement for slaughter:

A. Acceptable Daily Intake and Tolerances for Residues

The acceptable daily intake (ADI) for total residues of ractopamine hydrochloride is 1.25 micrograms *per* kilogram of body weight *per* day. The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product. A tolerance of 0.09 parts *per* million (ppm) is established for ractopamine hydrochloride (the marker residue) in liver (the target tissue), and 0.03 ppm in muscle, under 21 CFR 556.570.

The ADI for total residues of monensin is 12.5 micrograms *per* kilogram of body weight *per* day. The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product. A tolerance of 0.10 ppm is established for residues of monensin (the marker residue) in liver, and 0.05 ppm in muscle, kidney and fat, under 21 CFR 556.420.

An ADI is not cited for total residues of tylosin. The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product. A tolerance of 0.2 ppm is established for residues of tylosin (the marker residue) in fat, muscle, liver and kidney, under 21 CFR 556.740.

B. Withdrawal Period

Consistent with 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. Tissue residue studies are not required for the approval of the generic feed use combinations (Type B or Type C medicated feeds).

To this end, the withdrawal period for the generic combination Type B and Type C medicated feeds are those previously assigned to the RLNAD feed use combination. When used together, Optaflexx™ (ractopamine Type A medicated article), Monovet® (monensin Type A medicated article), and Tylovet® (tylosin phosphate) are approved with a 0-day withdrawal period.

C. Analytical Method for Residues

The validated analytical methods for analysis of residues of ractopamine, monensin, and tylosin are on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855. To obtain a copy of the analytical method, please submit a Freedom of Information request to: https://www.accessdata.fda.gov/scripts/foi/FOIRequest/requestinfo.cfm.

VI. USER SAFETY

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

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

The active ingredient in Optaflexx, 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 Optaflexx 45 formulation (Type A Medicated Article) poses a low dust potential under usual conditions of handling and mixing. When mixing and handling Optaflexx, use protective clothing, impervious gloves, protective eyewear, 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, call 1-800-428-4441.

VII. AGENCY CONCLUSIONS

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the FD&C Act and demonstrates that Optaflexx™, Monovet®, and Tylovet®, when used according to the label, are safe and effective.

Additionally, data demonstrate that residues in food products derived from cattle fed in confinement for slaughter administered Optaflexx™, Monovet®, and Tylovet® will not represent a public health concern when the combination medicated feed is used according to the label.