

Date of Approval: February 1, 2021

FREEDOM OF INFORMATION SUMMARY
ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-686

Optigrid[®] and Monovet[®] and Tylovet[®] and CycleGuard[®]

**(ractopamine hydrochloride Type A medicated article and
monensin Type A medicated article and tylosin phosphate and
melengestrol acetate Type A liquid medicated article)**

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

Heifers 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

Table of Contents

I. GENERAL INFORMATION.....	3
II. BIOEQUIVALENCE	5
III. HUMAN FOOD SAFETY	5
IV. USER SAFETY.....	6
V. AGENCY CONCLUSIONS.....	7

I. GENERAL INFORMATION

A. File Number

ANADA 200-686

B. Sponsor

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

Drug Labeler Code: 016592

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

C. Proprietary Name

Optigrid[®] and Monovet[®] and Tylovet[®] and CycleGuard[®]

D. Drug Product Established Name

ractopamine hydrochloride Type A medicated article and monensin Type A medicated article and tylosin phosphate and melengestrol acetate Type A liquid medicated article

E. Pharmacological Categories

Optigrid[®]: Beta adrenergic agonist
Monovet[®]: Ionophore, anticoccidial
Tylovet[®]: Antibacterial
CycleGuard[®]: Steroid hormone

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 Products¹

Optigrid[®]: 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
CycleGuard[®]: 500 mg/lb of melengestrol acetate

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 are the subject of this approval.

H. How Supplied

Optigrid®: 25 lb (11.34 kg) bags
Monovet®: 25 kg (55.12 lb) bags
Tylovet®: 50 lb (22.68 kg) bags
CycleGuard®: 40 lb (18 kg) (4.627 gal [17.5L]) container

I. Dispensing Status

Veterinary feed directive (VFD)

J. Route of Administration

Oral

K. Species/Class

Heifers fed in confinement for slaughter

L. Indications and Dosage Regimens

1. For increased rate of weight gain, improved feed efficiency, increased carcass leanness, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*, reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Arcanobacterium (Actinomyces) pyogenes*, and suppression of estrus (heat) in heifers fed in confinement for slaughter for the last 28 to 42 days on feed.
 - a. 9.8 to 24.6 g/ton to provide 90 to 430 mg/head/day of ractopamine hydrochloride (as Optigrid®) for increased rate of weight gain, improved feed efficiency and increased carcass leanness.
 - b. 10 to 40 g/ton to provide 0.14 to 0.42 mg/lb body weight per day, depending on the severity of the coccidiosis challenge, up to 480 mg/head/day, of monensin (as Monovet®) for improved feed efficiency and for the prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii*.
 - c. 8 to 10 g/ton to provide 60 to 90 mg/head/day of tylosin phosphate (as Tylovet®) for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Arcanobacterium (Actinomyces) pyogenes*.
 - d. 0.125 to 1.0 mg/lb fed at the rate of 0.5 to 2.0 lb/head/day to provide 0.25 to 0.5 mg/head/day of melengestrol acetate (as CycleGuard®) for increased rate of weight gain, improved feed efficiency and suppression of estrus (heat).

Feed continuously as sole ration for the final 28 to 42 days on feed.

Increased benefit for improved feed efficiency, when Optigrid®, Monovet®, and CycleGuard® are used together vs. individually and increased benefit for increased rate of weight gain, when Optigrid® and CycleGuard® 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 141-233.

M. Reference Listed New Animal Drug Combination (RLNAD)

Optaflexx™ and Rumensin™ and Tylan™ and MGA® (ractopamine hydrochloride Type A medicated article and monensin Type A medicated article and tylosin phosphate and melengestrol acetate Type A medicated article); NADA 141-233; Elanco US Inc.

N. Approved Original Generic Type A Medicated Article

CycleGuard®; melengestrol acetate Type A liquid medicated article; ANADA 200-399; Huvepharma EOOD

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

Optigrd® (ractopamine hydrochloride Type A medicated article); ANADA 200-679; Huvepharma EOOD
Monovet® (monensin Type A medicated article); ANADA 200-639; Huvepharma EOOD
Tylovet® (tylosin phosphate); ANADA 200-484; Huvepharma EOOD
CycleGuard® (melengestrol acetate Type A liquid medicated article); ANADA 200-399; Huvepharma EOOD

II. BIOEQUIVALENCE

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, allows for an abbreviated new animal drug application (ANADA) to be submitted for a generic version of an approved new animal drug (RLNAD). Target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Following the approval of an ANADA for a generic Type A medicated article, CVM's fourth policy letter issued on November 2, 1989, with regard to the implementation of GADPTRA, entitles the generic sponsor to submit an ANADA for each feed use combination (Type B or C medicated feed) for which the RLNAD is approved, without additional bioequivalence and tissue residue studies. CVM's fourth policy letter reaffirms that bioequivalence and tissue residues for each generic drug in the combination were adequately established in the ANADA at the time of its approval. Ractopamine hydrochloride is codified under 21 CFR 558.500, monensin is codified under 21 CFR 558.355, tylosin phosphate is codified under 21 CFR 558.625, melengestrol acetate is codified under 21 CFR 558.342. The combination of ractopamine hydrochloride, monensin, tylosin phosphate, and melengestrol acetate is codified under 21 CFR 558.625.

III. HUMAN FOOD SAFETY

The following are assigned to this product for heifers 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 (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 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 in fat, muscle, liver and kidney, under 21 CFR 556.740.

An ADI is not cited for total residues of melengestrol. The tolerances established for the feed use RLNAD apply to the generic feed use combination new animal drug product. A tolerance of 25 parts *per* billion (ppb) is established for residues of melengestrol in fat, under 21 CFR 556.380.

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 C medicated feeds are those previously assigned to the RLNAD feed use combination. When used together, Optigrin® (ractopamine Type A medicated article), Monovet® (monensin Type A medicated article), Tylovet® (tylosin phosphate), and CycleGuard® (melengestrol acetate Type A liquid medicated article) are approved with a 0-day withdrawal period.

C. Analytical Method for Residues

The validated analytical method for analysis of residues of ractopamine, monensin, tylosin, and melengestrol acetate 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>.

IV. USER SAFETY

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

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

The active ingredient in Optigrid[®], 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 Optigrid 45 formulation (Type A Medicated Article) poses a low dust potential under usual conditions of handling and mixing. When mixing and handling Optigrid, 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, call 1-877-994-4883.

V. AGENCY CONCLUSIONS

The information submitted in support of this ANADA satisfies the requirements of section 512(n) of the FD&C Act and demonstrate that Optigrid[®], Monovet[®], Tylovet[®] and CycleGuard[®], when used according to the label, are safe and effective for the indications listed in Section I.L. Additionally, data demonstrate that residues in food products derived from heifers fed in confinement for slaughter administered Optigrid[®], Monovet[®], Tylovet[®], and CycleGuard[®] will not represent a public health concern when the combination medicated feed is used according to the label.