

Date of Approval: July 18, 2014

FREEDOM OF INFORMATION SUMMARY
ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-559

ACTOGAIN 45 plus RUMENSIN

ractopamine hydrochloride plus monensin USP

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

**Cattle Fed in Confinement for Slaughter during the last 28 to 42
days on feed**

For increased rate of weight gain, improved feed efficiency, increased carcass leanness and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

Sponsored by:

Zoetis Inc.

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I. GENERAL INFORMATION:

A. File Number

ANADA 200-559

B. Sponsor

Zoetis Inc.
333 Portage St.
Kalamazoo, MI 49007

Drug Labeler Code: 054771

C. Proprietary Name

ACTOGAIN 45 plus RUMENSIN

D. Established Name

Ractopamine hydrochloride plus monensin USP

E. Pharmacological Category

Ractopamine hydrochloride – beta-adrenergic agonist
Monensin USP – ionophore/anticoccidial

F. Dosage Form

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

G. Amount of Active Ingredient in Currently Marketed Products*

Ractopamine hydrochloride – 45.4 g/lb
Monensin USP – 90.7 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

ACTOGAIN (ractopamine hydrochloride) 45– 25 lb (11.34 kg) bag
RUMENSIN (monensin USP) – 25 kg (55.12 lbs) bag

I. Dispensing Status

OTC

J. Dosage Regimen

There are three approved dosage regimens:

Ractopamine and Monensin:

Feed continuously as the sole ration at a concentration of 8.2 to 24.6 g of ractopamine hydrochloride per ton of complete feed to provide 70 to 430 mg/hd/day ractopamine for the last 28 to 42 days on feed.

Monensin is added to the ration at a concentrations of 10 to 40 g of monensin USP per ton of complete feed at a rate of 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 of monensin.

Ractopamine and Monensin Plus:

Feed continuously as the sole ration at a concentration of 9.8 to 24.6 g of ractopamine hydrochloride per ton of complete feed to provide 90 to 430 mg/hd/day ractopamine for the last 28 to 42 days on feed.

Monensin is added to the ration at a concentrations of 10 to 40 g of monensin USP per ton of complete feed at a rate of 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 of monensin.

Ractopamine top dress for complete feeds containing monensin:

Feed continuously as a Type C Top Dress at a minimum of 1.0 lb/head/day to cattle in confinement for slaughter, to provide 70 to 400 mg/head/day ractopamine for the last 28 to 42 days on feed, with a complete feed containing 10 to 40 g/ton monensin, 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.

K. Route of Administration

Oral, in feed

L. Species/Class

Cattle fed in confinement for slaughter

M. Indications

Amount: Ractopamine hydrochloride (8.2 to 24.6 g/ton) in combination with monensin USP (10 to 40 g/ton): For increased rate of weight gain, improved feed efficiency and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

Amount: Ractopamine hydrochloride (9.8 to 24.6 g/ton) in combination with monensin, USP (10 to 40 g/ton): For increased rate of weight gain, improved feed

efficiency, increased carcass leanness and prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

Amount: Ractopamine (not to exceed 800 g/ton) in combination with a complete feed containing monensin USP (10 to 40 g/ton): For increased rate of weight gain and improved feed efficiency, prevention and control of coccidiosis due to *Eimeria bovis* and *E. zuernii* in cattle fed in confinement for slaughter during the last 28 to 42 days on feed.

N. Approved Original Generic Type A Medicated Article

ACTOGAIN 45; ractopamine hydrochloride; ANADA 200-548; Zoetis Inc.

O. Reference Listed New Animal Drug

OPTAFLEXX plus RUMENSIN; ractopamine hydrochloride plus monensin USP; NADA 141-225; 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 are:

OPTAFLEXX; ractopamine hydrochloride; NADA 141-221; Elanco Animal Health, A Division of Eli Lilly & Co.

RUMENSIN; monensin USP; NADA 095-735; 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 monensin USP is codified under 21 CFR 558.355. The combination of ractopamine hydrochloride and monensin USP is codified under 21 CFR 558.500(e)(2).

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:

A. Tolerances for Residues:

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

The tolerance for ractopamine hydrochloride (the marker residue) is 0.09 parts per million (ppm) in the liver (the target tissue), and 0.03 ppm in the muscle, under 21 CFR 556.570(b)(1). The acceptable daily intake ADI for total residues of ractopamine hydrochloride is 1.25 micrograms per kilogram of body weight per day.

The tolerance for monensin is 0.1 ppm in the liver, and 0.05 ppm in the muscle, kidney, and fat, under 21 CFR 556.420(b)(1). The ADI for total residues of monensin is 12.5 micrograms per kilogram of body weight per day.

B. Withdrawal Periods:

Because a waiver from the requirement to demonstrate bioequivalence was granted for the Type A medicated article, ACTOGAIN 45, the withdrawal periods for the combination Type C medicated feeds are those previously assigned to the RLNAD product.

Ractopamine hydrochloride and monensin USP in combination are approved with a zero-day withdrawal period.

C. Regulatory Method for Residues:

The determination of residues of ractopamine in the liver and muscle of cattle, swine and turkeys is by High Performance Liquid Chromatography (HPLC). The confirmation of residues of ractopamine in the liver and muscle of cattle, swine and turkeys 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 regulatory analytical method for monensin is the method developed by Eli Lilly & Co., Box 708, Greenfield, IN 46140 (Method 5801654, "Determination of Monensin in Tissues and Eggs") on file at the Center for Veterinary Medicine, Food and Drug Administration, HFV-199, 7500 Standish Place, Rockville, Maryland 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.

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 ACTOGAIN 45 plus RUMENSIN, when used according to the label, is safe and effective.