Date of Approval: November 3, 2021

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-508

Experior™

Lubabegron Type A medicated article

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

Beef steers and heifers fed in confinement for slaughter

This supplement provides for addition of residue tolerances of 3 ppb in muscle and 20 ppb in kidney

Sponsored by:

Elanco US Inc.

Executive Summary

This supplemental approval of Experior™ (lubabegron Type A medicated article) provides for the addition of residue tolerances for muscle and kidney. Experior™ is already approved for reduction of ammonia gas emissions per pound of live weight and hot carcass weight in beef steers and heifers fed in confinement for slaughter ("feedlot" beef cattle) during the last 14 to 91 days on feed.

Proprietary Name	Established Name	Application Type and Number	Sponsor
Experior™	lubabegron Type A medicated article	New Animal Drug Application (NADA) 141-508	Elanco US Inc.

Lubabegron Type A medicated article is a mixed beta-adrenergic agonist-antagonist. In cattle, it has agonistic behavior at one beta-adrenergic receptor subtype and antagonistic behavior at two beta-adrenergic receptor subtypes. When fed to feedlot beef cattle, the drug reduces the amount of nitrogen that the animals excrete in their manure, leading to less ammonia gas released as a by-product of their waste.

Because Experior™ is a Type A medicated article, it cannot be fed undiluted to animals. A Type A medicated article is used to make another Type A medicated article or a Type B or Type C medicated feed. Only a Type C medicated feed can be fed directly to animals.

FDA approved Experior™ as an over-the-counter drug because the Agency determined that adequate "directions for use" can be written on the labeling in such a way that non-veterinarians can use the drug safely and effectively.

Safety and Effectiveness

The Freedom of Information (FOI) Summary for the original approval of Experior™ under NADA 141-508, dated November 6, 2018, contains summaries of the information used to assess the drug's safety and effectiveness in feedlot beef cattle.

Human Food Safety

Because lubabegron is approved for a food-producing animal, the use of the drug will result in residues in meat. In the FOI Summary for the original approval of Experior™, dated November 6, 2018, FDA established that liver is the target tissue to test for residues of lubabegron. The residue tolerance in cattle liver remains 10 parts per billion (ppb). The current supplemental approval adds residue tolerances for muscle at 3 ppb and for kidney at 20 ppb. This means that the highest concentration of lubabegron residues legally allowed in or on the liver, muscle, and kidney of treated cattle is 10 ppb, 3 ppb, and 20 ppb, respectively. FDA evaluated the validated analytical method to detect lubabegron residues in the edible tissues of cattle and found its use acceptable.

There is no change to the previously established acceptable daily intake or safe concentrations for total residues of lubabegron in individual edible tissues of beef

cattle. There is also no change to the previously established withdrawal period; it remains zero-day.

User Safety

The labeling for Experior™ describes the precautions people should take when mixing and handling the drug. People with heart disease should be especially careful to avoid exposure to lubabegron because of the drug's effects on the cardiovascular system.

Conclusions

Based on the data submitted by the sponsor for the approval of Experior™, FDA determined that the drug is safe and effective when used according to the labeling.

Table of Contents

I. GENERAL INFORMATION

A. File Number

NADA 141-508

B. Sponsor

Elanco US Inc.
2500 Innovation Way
Greenfield, IN 46140

Drug Labeler Code:

C. Proprietary Name

Experior™

D. Drug Product Established Name

Lubabegron Type A medicated article

E. Pharmacological Category

Beta adrenergic agonist/antagonist

F. Dosage Form

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

G. Amount of Active Ingredient[1]

Lubabegron (as lubabegron fumarate) - 10 g per kg (4.54 g per lb) and 50 g per kg (22.7 g per lb)

H. How Supplied

10 kg bags

I. Dispensing Status

Over-the-counter (OTC)

J. Dosage Regimen

Feed 1.25 to 4.54 g/ton (1.39 to 5 ppb) of complete feed (90% dry matter basis) to provide 13 – 90 mg lubabegron/head/day continuously to beef steers and

[1] The sponsor of this individual currently marketed Type A medicated article may have approvals for other strengths 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 this Type A medicated article. 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.

heifers fed in confinement for slaughter as the sole ration during the last 14 to 91 days on feed.

K. Route of Administration

Oral

L. Species/Class

Beef steers and heifers fed in confinement for slaughter

M. Indication

For reduction of ammonia gas emissions per pound of live weight and hot carcass weight in beef steers and heifers fed in confinement for slaughter during the last 14 to 91 days on feed.

N. Effect of Supplement

This supplement provides for addition of residue tolerances of 3 ppb in muscle and 20 ppb in kidney.

II. EFFECTIVENESS

A. Dosage Characterization

This supplemental approval does not change the previously approved dosage range. The Freedom of Information (FOI) Summary for the original approval of NADA 141-508 dated November 6, 2018 contains dosage characterization information for beef steers and heifers fed in confinement for slaughter.

B. Substantial Evidence

CVM did not require effectiveness studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-508 dated November 6, 2018 contains a summary of studies that demonstrate effectiveness of the drug for beef steers and heifers fed in confinement for slaughter.

III. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-508 dated November 6, 2018 contains a summary of studies that demonstrate effectiveness of the drug for beef steers and heifers fed in confinement for slaughter.

IV. HUMAN FOOD SAFETY

A. Microbial Food Safety

CVM did not require additional information for microbial food safety (antimicrobial resistance) for this supplemental approval.

B. Toxicology

Reassessment of the codified acceptable daily intake (ADI) was not needed for this supplemental approval. The codified ADI for total residue of lubabegron is 3 µg/kg of body weight per day, as listed under 21 CFR §556.370. The safe concentrations for total residues of lubabegron in individual edible tissues of beef cattle are 0.6 ppb for muscle, 1.8 ppb for liver, 3.6 ppb for kidney, and 3.6 ppb for fat.

The FOI Summary for the original approval of NADA 141-508, dated November 6, 2018, contains summaries of all toxicology studies and information.

C. Residue Chemistry

1. Summary of Residue Chemistry Studies

   CVM did not require residue chemistry studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-508 dated November 6, 2018, contains a summary of residue chemistry studies for cattle. The only additional data required was method validation information for the methods described in below in Section D.

2. Target Tissue and Marker Residue

   Reassessments of target tissue and marker residue were not needed for this supplemental approval. The marker residue for lubabegron is lubabegron and the target tissue in cattle is liver.

3. Tolerances

   Data provided in the original approval of NADA 141-508 support the assignment of tolerances for lubabegron in cattle of 3 ppb in muscle and 20 ppb in kidney. The tolerance in cattle liver (target tissue) remains 10 ppb.

4. Withdrawal Period and/or Milk Discard Time and/or Honey Discard Time

   This supplement does not result in any change to the previously established withdrawal period. The withdrawal period remains 0 days. Refer to the FOI Summary for the original approval of NADA 141-508 dated November 6, 2018.

D. Analytical Method for Residues

1. Description of Analytical Method

   a. Determinative Procedure

      After adding internal standard (LSN543100) to homogenized cattle muscle or kidney, the sample is extracted twice with methanol:acetonitrile, centrifuged, and brought to volume in methanol:acetonitrile. An aliquot is centrifuged, filtered, and analyzed by LC-MS/MS. Quantitation is based on the m/z 500 → m/z 250 and m/z 518 → m/z 250 transitions for lubabegron and LSN543100, respectively.

   b. Confirmatory Procedure

Sample extraction and LC-MS/MS analysis for the confirmatory procedure are identical to those for the determinative procedure. Lubabegron-specific ion transitions (m/z 500 → m/z 250, m/z 500 → m/z209, and m/z 500 → m/z 187) are monitored to obtain ion ratios, signal to noise ratios, and retention times that meet the required acceptability criteria.

2. Availability of the Method

The validated analytical method for analysis of residues of lubabegron Type A medicated article is 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.

V. USER SAFETY

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

User Safety Warning: The active ingredient in Experior, lubabegron, is a beta-adrenergic agonist/antagonist. Individuals with cardiovascular disease should exercise special caution to avoid exposure. Not for human use. Keep out of reach of children. When mixing and handling Experior, 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 thoroughly with water; if wearing contact lenses, rinse eyes first, then remove contact lenses and continue to rinse for 5-20 minutes. If irritation persists, seek medical attention. The safety data sheet contains more detailed occupational safety information. To report adverse drug events, access medical information, or obtain additional product information, call Elanco US Inc. at 1-800-428-4441. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR part 514. The data demonstrate that Experior™, when used according to the label, is safe and effective for reduction of ammonia gas emissions per pound of live weight and hot carcass weight in beef steers and heifers fed in confinement for slaughter during the last 14 to 91 days on feed. Additionally, data demonstrate that residues in food products derived from species treated with Experior™ will not represent a public health concern when the product is used according to the label.

A. Marketing Status

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the label are reasonably certain to be followed in practice.

B. Exclusivity

Experior™, as approved in our approval letter, does not qualify for marketing exclusivity under section 512(c)(2)(F) of the Federal Food, Drug, and Cosmetic Act.

C. Supplemental Applications

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(1)).

D. Patent Information

For current information on patents, see the Green Book Reports in the Animal Drugs @ FDA database.