Date of Approval: July 8, 2024

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-771

Felanorm®

(methimazole)

Oral solution

Cats

Felanorm® (methimazole) is indicated for the treatment of hyperthyroidism in cats.

Sponsored by:

Norbrook Laboratories Ltd.

Executive Summary

Felanorm® (methimazole) oral solution is approved for the treatment of hyperthyroidism in cats. The reference listed new animal drug (RLNAD) is Felimazole® Coated Tablets (methimazole tablets) sponsored by Dechra, Ltd., under NADA 141-292. This is the first generic methimazole oral solution for cats.

Bioequivalence

For this approval, the Food and Drug Administration (FDA) approved a suitability petition to allow the sponsor to submit an abbreviated new animal drug application (ANADA) for a generic animal drug that differs in dosage form from the RLNAD. Suitability petition FDA-2018-P-2985, approved on October 12, 2018, provides for the generic new animal drug as a methimazole oral solution containing 5 mg methimazole per 1 mL of solution. The RLNAD is a non-scored compressed coated tablet available in 2.5 mg and 5 mg tablet sizes. Felimazole® Coated Tablets may be dosed in whole tablet size increments only (2.5 mg increments). The generic methimazole oral solution will also be dosed in 2.5 mg increments, thereby providing the same approved dosage as the RLNAD.

The sponsor conducted one *in vivo* blood-level study in cats to show that the 5 mg/mL Felanorm® oral solution is bioequivalent to the 5 mg Felimazole® Coated Tablets. No serious adverse events were reported during the study.

Conclusions

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

Table of Contents

I. GENERAL INFORMATION

A. File Number

ANADA 200-771

B. Sponsor

Norbrook Laboratories Ltd.
Carnbane Industrial Estate
Newry, County Down
BT35 6QQ, United Kingdom

Drug Labeler Code: 055529

C. Proprietary Name

Felanorm®

D. Drug Product Established Name

methimazole

E. Pharmacological Category

Antithyroid

F. Dosage Form

Oral solution

G. Amount of Active Ingredient

5 mg/mL

H. How Supplied

30 mL or 100 mL bottles with 1 mL and 5 mL dosing syringes

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

The starting dose of Felanorm® is 2.5 mg administered every 12 hours. Following 3 weeks of treatment, the dose should be titrated to effect based on individual serum total T4 (TT4) levels and clinical response. Dose adjustments should be made in 2.5 mg increments. The maximum total dosage is 20 mg per day divided, not to exceed 10 mg as a single administration.

K. Route of Administration

Oral

L. Species/Class

Cats

M. Indication

Felanorm® (methimazole) is indicated for the treatment of hyperthyroidism in cats.

N. Reference Listed New Animal Drug

Felimazole® Coated Tablets; methimazole tablets; NADA 141-292; Dechra, Ltd.

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). The ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. Effectiveness, target animal safety and human food safety data (other than tissue residue data) are not required for approval of an ANADA. If bioequivalence is demonstrated through a clinical endpoint study in a food-producing animal, then a tissue residue study to establish the withdrawal period for the generic product is also required.

The sponsor submitted a suitability petition (FDA-2018-P-2985) requesting permission to submit an ANADA for a generic new animal drug that differed in dosage form from the RLNAD. The generic drug is a methimazole oral solution containing 5 mg methimazole per 1 mL of solution. The RLNAD is a non-scored compressed coated tablet available in 2.5 and 5 mg tablet sizes. This petition was approved on October 12, 2018, under 512(n)(3)(C) of the FD&C Act.

For this ANADA, one *in vivo* blood-level study was conducted to demonstrate product bioequivalence using the generic 5 mg/mL oral solution and RLNAD 5 mg methimazole tablet. The RLNAD is available in 2.5 and 5.0 mg tablet sizes. The *in vivo* blood-level study was conducted in 32 healthy fasted cats. The pivotal parameters to evaluate bioequivalence are the observed maximum plasma drug concentration (C_{MAX}) and area under the concentration-time curve (AUC) from time 0 to the last sampling time before the first unquantifiable concentration after C_{MAX}. Bioequivalence was demonstrated between the 5 mg RLNAD methimazole tablet and the 5 mg/mL methimazole oral solution by the average bioequivalence approach as described in the Statistical Methods section below. The study information is summarized below.

A. Blood-level Bioequivalence Study in Cats

Title: A Pharmacokinetic Study to Determine the Plasma Levels of Methimazole in Cats Following the Oral Administration of Methimazole Oral Solution (Norbrook Laboratories Ltd, Product code: O-MET-010) and Felimazole 5 mg Coated Tablets for Cats. (Study No. 004/22)

Study Dates: April 25, 2022 to November 17, 2023

Study Locations:

In-life phase: Rostrevor, Co. Down, Northern Ireland

Bioanalytical testing: Barcelona, Spain

Study Design:

Objective: The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence data for the generic 5 mg/mL Felanorm® (methimazole) oral solution and the 5 mg RLNAD Felimazole® Coated Tablets (methimazole tablets) in fasted cats.

Study Animals: Thirty-two healthy intact and neutered male and female cats between 1 and 14 years old and weighing between 3.46 kg to 6.79 kg.

Experimental Design: A randomized, masked, two-period, two-treatment, two-sequence, single-dose crossover study conducted according to Good Laboratory Practice for Nonclinical Laboratory Studies.

Drug Administration: Each animal received 5 mg of either the generic or RLNAD methimazole according to their randomized treatment sequence (generic/RLNAD or RLNAD/generic).

Measurements and Observations: The plasma concentrations of methimazole were measured using a validated bioanalytical method. Pharmacokinetic parameters were determined for each animal individually in each period. Animal observations were made throughout the study for assessment of general health and adverse events.

Statistical Methods:

The laboratory study was conducted with a randomized, masked, two-period, two-sequence, two-treatment, single-dose crossover design using 32 cats with a 42-day washout between periods. Appropriate randomization of animal to sequence, set and pen/treatment order was performed. Primary variables evaluated were C_{MAX} and AUC. Time to maximum concentration (T_{MAX}) was summarized and evaluated clinically.

A mixed-effect model was used to evaluate bioequivalence. The model included fixed effects of treatment, sequence and period, and random effects of pen, set and subject nested within sequence and set. Prior to the analysis, C_{MAX} and AUC were natural logarithm transformed. Bioequivalence is established because the back-transformed estimated upper and lower bounds of the 90 percent confidence interval for geometric mean ratios (generic/RLNAD) of both C_{MAX} and AUC are contained within the acceptance limits of 0.80 to 1.25.

Results:

As seen in the table below, C_{MAX} and AUC fall within the prescribed bounds (Table II.1). The mean values of T_{MAX} obtained for the generic article and RLNAD were summarized.

Table II.1. Bioequivalence Evaluation

Parameter	Generic Mean	RLNAD Mean	Ratio◊	Lower 90% CI	Upper 90% CI
AUC (ng/mL)*hour	6416.3†	6948.5†	0.92	0.88	0.97
C_{MAX} (ng/mL)	1457.5†	1569.8†	0.93	0.87	0.99
T_{MAX} (hours) (SD)‡	0.47 (0.26)‡	0.54 (0.42)‡	NE	NE	NE

† Geometric mean
‡ Arithmetic mean and standard deviation (SD)
◊ Ratio = Generic:RLNAD
CI = confidence interval
NE = not estimated

Adverse Reactions:

There were no serious adverse events reported during the study.

Conclusion:

The *in vivo* bioequivalence study demonstrated that the generic 5 mg/mL Felanorm® (methimazole) oral solution and the RLNAD 5 mg Felimazole® Coated Tablets (methimazole tablets) are bioequivalent in cats.

III. HUMAN FOOD SAFETY

This drug is intended for use in cats. Because this new animal drug is not intended for use in food-producing animals, the Center for Veterinary Medicine did not require data pertaining to drug residues in food (i.e., human food safety) for approval of this ANADA.

IV. USER SAFETY

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

HUMAN WARNINGS: Not for use in humans. Keep out of reach of children. For use in cats only. Wear protective single use, impermeable (e.g., latex or nitrile) gloves when administering the solution. Wash hands with soap and water after administration to avoid exposure to drug. Wear protective gloves to prevent direct contact with litter, feces, urine, or vomit of treated cats, and the solution. Wash hands after contact with the litter of treated cats.

Methimazole is a human teratogen and crosses the placenta concentrating in the fetal thyroid gland. There is also a high rate of transfer into breast milk. Pregnant women or women who may become pregnant, and nursing mothers should wear gloves when

handling the solution, litter or bodily fluids of treated cats. Individuals with an endocrine disorder that could be impacted by methimazole should use similar precautions.

Methimazole may cause vomiting, gastric distress, headache, fever, arthralgia, pruritus, and pancytopenia. In the event of accidental ingestion/overdose, seek medical advice immediately and show the product label to the physician.

Avoid skin and oral exposure, including hand-to-mouth contact. Wash any spillages or splatter from the skin immediately. Do not eat, drink, smoke/vape, or use smokeless tobacco while handling the product or used litter.

Felanorm® may cause skin or eye irritation. Avoid eye contact, including hand-to-eye contact. In case of accidental eye contact, rinse eyes immediately with clean running water. If irritation develops, seek medical advice.

V. AGENCY CONCLUSIONS

The data submitted in support of this ANADA satisfy the requirements of section 512(c)(2) of the FD&C Act. The data demonstrate that Felanorm®, when used according to the label, is safe and effective for the conditions of use in the General Information Section above.