Date of Approval: June 27, 2025

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA)

ANADA 200-814

Methimazole Coated Tablets

(methimazole tablets)

Cats

Methimazole Coated Tablets (methimazole tablets) are indicated for the treatment of hyperthyroidism in cats.

Sponsored by:

Felix Pharmaceuticals Pvt. Ltd.

Executive Summary

Methimazole Coated Tablets (methimazole tablets) 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 tablet for cats.

Bioequivalence

The sponsor conducted one *in vivo* blood-level study in cats to demonstrate that the 5 mg Methimazole Coated Tablets (methimazole tablets) is bioequivalent to the 5 mg Felimazole® Coated Tablets (methimazole tablets). No serious adverse events were reported during the study.

The sponsor conducted a comparative *in vitro* dissolution study for the additional product strengths. Based on the dissolution data, the 2.5 mg Methimazole Coated Tablets (methimazole tablets) qualified for a waiver from the requirement to perform separate *in vivo* bioequivalence studies (a biowaiver). The Food and Drug Administration (FDA) granted a biowaiver for these strengths.

Conclusions

Based on the data submitted by the sponsor for the approval of Methimazole Coated Tablets, 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 200-814

B. Sponsor

Felix Pharmaceuticals Pvt. Ltd.
25-28 North Wall Quay
Dublin 1, Ireland

Drug Labeler Code: 086101

U.S. Agent Name and Address:

Sreejith Kurup
Felixvet Inc.
1300 NW Briarcliff Parkway
Suite 100
Kansas City, MO 64150

C. Proprietary Name

Methimazole Coated Tablets

D. Drug Product Established Name

methimazole tablets

E. Pharmacological Category

Antithyroid

F. Dosage Form

Coated tablet

G. Amount of Active Ingredient

2.5 mg or 5 mg methimazole per tablet

H. How Supplied

100 count bottles

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

The starting dose of Methimazole Coated Tablets 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

Methimazole Coated Tablets (methimazole tablets) are 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.

For this ANADA, one *in vivo* blood-level study was conducted to demonstrate product bioequivalence using the generic and RLNAD methimazole tablets 5 mg. The RLNAD is available in 2.5 mg and 5 mg coated tablet sizes. The *in vivo* blood-level study was conducted in 30 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 generic methimazole tablet and the 5 mg RLNAD methimazole tablet by the average bioequivalence approach as described in the Statistical Method section below. The study information is summarized below.

A. Blood-level Bioequivalence Study in Cats

Title: Pivotal Bioequivalence Study of Generic Methimazole Tablets (5 mg) versus Felimazole® Coated Tablets (methimazole tablets) 5 mg When Administered Orally to Cats Under Fasted Conditions. (Study No. 080-BF-2033)

Study Dates: June 19, 2023 to November 28, 2023

Study Locations:

In-life phase: Ontario, Canada

Bioanalytical testing: Ontario, Canada

Study Design:

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

Study Animals: Thirty healthy, non-pregnant intact female, and neutered male and female cats, between 6 months and 5 years of age, and between 3.5 – 5.5 kg of weight.

Experimental Design: A randomized, masked, two-period, 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 tablets 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 Method:

The laboratory study was conducted as a randomized, masked, two-period, two-sequence, two-treatment, single-dose crossover design using 30 cats with a 14-day washout between periods. Appropriate randomization of animal to sequence 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 a random effect of subject nested within sequence. 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% 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	26605†	26493†	1.00	0.98	1.03
C_{MAX} (ng/mL)	1418†	1407†	1.01	0.97	1.05
T_{MAX} (hours) (SD)‡	1.25 (1.31)‡	1.02 (0.80)‡	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 Methimazole Coated Tablets and the RLNAD 5 mg Felimazole® Coated Tablets (methimazole tablets) are bioequivalent in cats.

B. Bioequivalence Waiver

A pivotal *in vivo* blood bioequivalence study was conducted using the 5.0 mg methimazole coated tablet strength. A waiver from the requirement to perform *in vivo* bioequivalence studies (biowaiver) for the generic 2.5 mg coated tablet was requested. To qualify for a biowaiver for each of these product strengths, comparative *in vitro* dissolution studies were conducted to determine the dissolution profiles of the generic and RLNAD 5.0 mg and 2.5 mg methimazole coated tablets. Comparisons were made between the following tablets:

- Generic 5.0 mg and generic 2.5 mg tablets
- Generic 5.0 mg and RLNAD 5.0 mg tablets
- Generic 5.0 mg and RLNAD 2.5 mg tablets

The objective was to demonstrate sameness of the generic tablet strengths (5.0 and 2.5 mg), as well as sameness of the generic tablet strengths to the corresponding RLNAD tablet strengths.

Test conditions were as follows:
- Dissolution apparatus: USP Apparatus I
- Dissolution medium: Water
- Dissolution medium volume: 500 mL
- Temperature: 37 °C ± 0.5 °C
- Paddle speed: 100 rpm
- Number of vessels: 12

- Data points: 5, 10, 15, 20, 30, and 45 minutes

The generic drug lot number used in the *in vivo* bioequivalence study was the same lot used to support the *in vitro* profile comparisons. Analytical method validation was required to ensure that the quantification of drug concentrations in all samples was accurate and precise.

To allow use of mean data, the percent coefficient of variation at the earlier time points (e.g., 15 minutes) should not be more than 20%, and at other time points should not be more than 10%. The percent coefficient of variation for all generic product profiles was within acceptable limits. Only one measurement should be considered after 85% dissolution of one of the products. The similarity factor (f_2) should be greater than 50 to ensure sameness or equivalence of two profiles.

The Center for Veterinary Medicine (CVM) estimated f_2 metrics based on mean data, and a summary of the results is presented in table II.2. below:

Table II.2. Similarity Results

Dissolution Comparison	Similarity Results
Generic 5.0 mg* to Generic 2.5 mg	>85% dissolved in 15 minutes
Generic 5.0 mg* to RLNAD 2.5 mg	>85% dissolved in 15 minutes
Generic 5.0 mg* to RLNAD 5.0 mg	>85% dissolved in 15 minutes

*Generic product lot used in the *in vivo* bioequivalence study

Study results demonstrate similar dissolution profiles for all comparisons. However, because of rapid dissolving characteristics (>85% in 15 minutes) in all strengths, a dissolution profile comparison using the f_2 test is unnecessary. When comparative profiles between tablets do not require an f_2 test because of rapid dissolution or when the f_2 value is ≥50, the product strengths used in the comparison qualify for a biowaiver. Therefore, a biowaiver for the generic 2.5 mg methimazole coated tablet is granted.

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, CVM 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 Methimazole Coated Tablets:

HUMAN WARNINGS: Not for use in humans. Keep out of reach of children. For use in cats only. Wash hands with soap and water after administration to avoid exposure to drug. Do not break or crush tablets. Wear protective gloves to prevent direct contact with litter, feces, urine, or vomit of treated cats, and broken or moistened tablets. 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 tablets, litter or bodily fluids of treated cats.

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.

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 Methimazole Coated Tablets, when used according to the label, is safe and effective for the conditions of use in the General Information Section above.