Date of Approval: May 1, 2015

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-497

LOXICOM

Meloxicam

Oral Suspension

Dogs

For the control of pain and inflammation associated with osteoarthritis in dogs.

Sponsored by:

Norbrook Laboratories, Ltd.

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I. GENERAL INFORMATION:

A. File Number

ANADA 200-497

B. Sponsor

Norbrook Laboratories, Ltd.
Station Works
Newry BT35 6JP
Northern Ireland

Drug Labeler Code: 055529

US Representative Name and Address

S. Lee Whaley, M.S.
Norbrook, Inc.
9733 Loiret Boulevard
Lenexa, KS 66219

C. Proprietary Name

LOXICOM

D. Product Established Name

meloxicam

E. Pharmacological Category

Non-steroidal anti-inflammatory

F. Dosage Form:

Oral suspension

G. Amount of Active Ingredient

1.5 mg/mL

H. How Supplied

10 mL, 32 mL, and 100 mL bottles with small and large dosing syringes

I. Dispensing Status

Rx

J. Dosage Regimen

On the first day of treatment, administer 0.09 mg/lb (0.2 mg/kg).
For all treatments after day 1, administer once daily at a dose of 0.045 mg/lb (0.1 mg/ kg).

K. Route of Administration

Oral

L. Species/Class

Dogs

M. Indication

For the control of pain and inflammation associated with osteoarthritis in dogs.

N. Reference Listed New Animal Drug

METACAM; meloxicam; NADA 141-213; Boehringer Ingelheim Vetmedica, Inc.

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 or RLNAD). 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. Information to show that the generic version is bioequivalent to the approved RLNAD is required for approval.

For this ANADA, an *in vivo* blood-level study was conducted using the test and reference 1.5 mg/mL meloxicam oral suspension to demonstrate product bioequivalence. The following blood-level bioequivalence study demonstrated that the generic product was bioequivalent to the approved RLNAD.

a. Title:

A pharmacokinetic study to determine the plasma levels of meloxicam in dogs following the oral administration of Meloxicam 1.5 mg/ml Oral Suspension for Dogs (Norbrook Laboratories Limited, Product Code O-MELOX-010) and Metacam Oral Suspension (Boehringer Ingelheim Vetmedica, Inc, NADA 141-213).

b. Investigator:

Study Director:
Cormac Caraher, B.Sc.

In-life test facility:
Ballyedmond Castle Farms Ltd
Rostrevor
County Down BT34 3AG
Northern Ireland

Analytical test facility:
Norbrook Laboratories, Ltd.
Station Works
Newry BT35 6JP
Northern Ireland

c. Study Design:

1) Objective:
To evaluate blood-level bioequivalence of the generic meloxicam oral suspension 1.5 mg/mL (Norbrook Laboratories, Ltd.) to METACAM Oral Suspension 1.5 mg/mL (Boehringer Ingelheim Vetmedica, Inc.), NADA 141-213.

2) Study Animals:
Eighteen healthy Beagle dogs; six female and twelve male dogs
Age range: 1.5 to 8 years
Weight: 11.0 to 16.1 kg.

3) Experimental Design:
The study was conducted as a two-period, two-treatment, crossover design with a 35-day washout time between study periods. In each period, blood samples were collected from each animal before treatment administration and at 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 5, 7, 9, 12, 24, 48, 72, 96, and 120 hours post dose. In total, 17 blood samples were taken from each dog during each treatment period.

4) Drug Administration:
In each period, each animal was orally administered either METACAM Oral Suspension (reference article) or the generic meloxicam oral suspension (test article) at a dose of 0.2 mg meloxicam/kg bodyweight. This dose was administered rounded to the nearest gradation of the syringe.

5) Measurements and Observations:
The concentrations of meloxicam were measured using a validated high performance liquid chromatography (HPLC) method. Pharmacokinetic parameters were determined for each animal individually in each period.

d. Statistical Methods:
Blood level bioequivalence was based on two decision variables, the area under the concentration curve (AUC) from time 0 to the last value measured above the lower limit of quantification, and maximum concentration (C_{MAX}). The time at which C_{MAX} is reached in the blood stream (T_{MAX}) was summarized and clinically evaluated, but no confidence intervals were estimated.

AUC and C_{MAX} were logarithmically (natural log) transformed for analysis to log-transformed AUC (LAUC) and log-transformed C_{MAX} (LC_{MAX}), respectively. A linear mixed effects model containing treatment, sequence, period, and treatment-by-period interaction as fixed effects, and dog-within-sequence as a random effect was used to analyze LC_{MAX} and LAUC. Confidence intervals for the ratio of the two treatments were based on back-transforming the endpoints of the 90% confidence interval for the difference between the two

treatments for both LAUC and LC_{MAX}. The endpoints were compared to the acceptance range of 80% to 125% for bioequivalence evaluation.

e. Results:

No statistically significant effects (α =0.05) for fixed effects were detected in the analysis of LAUC or LC_{MAX}. T_{MAX} was assessed by clinical evaluation.

The following table provides the back-transformed results for AUC and $C_{MAX,}$ and the arithmetic means for T_{MAX}.

Variable	Test (LOXICOM)	Reference (METACAM)	Lower Bound	Upper Bound
AUC (mg/mL)*hour	22.7258*	23.5141*	87.01%	107.34%
C_{MAX} (mg/L)	0.6023*	0.6383*	87.24%	102.07%
T_{MAX} (hour)	5.7†	3.0†	NA	NA

*Geometric Mean
†Arithmetic Mean

f. Conclusion:

Bioequivalence criteria are met for LOXICOM for both AUC (87% to 107%) and C_{MAX} (87% to 102%). The T_{MAX} values obtained for the test and reference products indicate that these drugs should provide equivalent therapeutic results.

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:

Data on human food safety, pertaining to drug residues in food, were not required for approval of this application. This drug is approved for use in dogs, which are not food producing animals.

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 LOXICOM:

> Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. For oral use in dogs only.

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 LOXICOM, when used according to the label, is safe and effective.