

Date of Approval: July 29, 2022

FREEDOM OF INFORMATION SUMMARY
ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-726

Firocoxib Tablets for Horses

(firocoxib)

Horses

Firocoxib Tablets for Horses are administered once daily for up to 14 days for the control of pain and inflammation associated with osteoarthritis in horses.

Sponsored by:

Pegasus Laboratories, Inc.

Executive Summary

Firocoxib Tablets for Horses (firocoxib) are approved for administration once daily for up to 14 days for the control of pain and inflammation associated with osteoarthritis in horses. Firocoxib Tablets for Horses are a generic version of Equioxx[®] (firocoxib) Tablets.

	Proprietary Name	Established Name	Application Type and Number	Sponsor
Generic Animal Drug	Firocoxib Tablets for Horses	firocoxib	Abbreviated New Animal Drug Application (ANADA) 200-726	Pegasus Laboratories, Inc.
Brand Name Animal Drug, also called the Reference Listed New Animal Drug (RLNAD)	Equioxx [®] Tablets	firocoxib	New Animal Drug Application (NADA) 141-458	Boehringer Ingelheim Animal Health USA, Inc.

Firocoxib is in the coxib class of non-narcotic, non-steroidal anti-inflammatory drugs (NSAIDs). Like many NSAIDs, firocoxib works by inhibiting the enzyme cyclooxygenase, which in turn, leads to decreased synthesis of prostaglandins. Prostaglandins contribute to pain, fever, and inflammation throughout the body, among other functions.

Bioequivalence

The Federal Food, Drug, and Cosmetic (FD&C) Act allows an animal drug sponsor to submit an abbreviated new animal drug application (ANADA) for a generic version of an approved brand name animal drug (also called the reference listed new animal drug or RLNAD). This law typically requires the sponsor to show that the generic drug is bioequivalent to the approved RLNAD. Broadly, bioequivalence means the generic drug is absorbed by and performs the same way in the animal's body as the RLNAD, which has already been shown to be safe and effective when used according to the label. The FD&C Act doesn't require the sponsor to submit new effectiveness or target animal safety data in the ANADA for a generic animal drug.

The sponsor conducted one *in vivo* blood-level study in healthy, fasted horses to show that the 57 mg Firocoxib Tablets for Horses are bioequivalent to the 57 mg Equioxx[®] tablets. No serious adverse events were reported during the study.

Conclusions

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

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I. GENERAL INFORMATION

A. File Number

ANADA 200-726

B. Sponsor

Pegasus Laboratories, Inc.
8809 Ely Rd.
Pensacola, FL 32514

Drug Labeler Code: 055246

C. Proprietary Name

Firocoxib Tablets for Horses

D. Drug Product Established Name

firocoxib

E. Pharmacological Category

Non-steroidal anti-inflammatory

F. Dosage Form

Tablet

G. Amount of Active Ingredient

57 mg firocoxib per tablet

H. How Supplied

Round, half-scored tablets in 60-count bottles

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

One 57 mg tablet administered orally to horses weighing 800 – 1300 lbs, once daily for up to 14 days.

K. Route of Administration

Oral

L. Species/Class

Horses

M. Indication

Firocoxib Tablets for Horses are administered once daily for up to 14 days for the control of pain and inflammation associated with osteoarthritis in horses.

N. Reference Listed New Animal Drug (RLNAD)

Equioxx[®] Tablets; firocoxib; NADA 141-458; Boehringer Ingelheim Animal Health USA, Inc.

II. BIOEQUIVALENCE

The FD&C Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, allows for an ANADA to be submitted for a generic version of an approved 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 firocoxib 57 mg tablets. The RLNAD is available in 57 mg tablets. The *in vivo* blood-level study was conducted in 24 healthy, fasted horses. 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 57 mg Equioxx[®] (firocoxib) tablets and the 57 mg Firocoxib Tablets for Horses by the mixed reference-scaled average bioequivalence approach as described in the Statistical Methods section below. The study information is summarized below.

Blood-level Bioequivalence Study in Horses

Title: Pivotal Bioequivalence Study of Equioxx[®] and a Generic Formulation of Firocoxib Tablets When Administered Orally to Horses (Study No. PLI-CL-043)

Study Dates: March 9, 2020 to December 8, 2020

Study Locations:

In-life phase: Las Cruces, NM

Bioanalytical testing: Colorado Springs, CO

Study Design:

Objective: The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence data for the generic 57 mg Firocoxib Tablets for Horses and the RLNAD 57 mg Equioxx[®] (firocoxib) Tablets in fasted horses.

Study Animals: Twenty-four healthy, male/castrated horses, ranging in age from 3 to 10 years, weighing between 969 and 1088 pounds.

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

Drug Administration: Each animal received 57 mg of either the generic or RLNAD firocoxib according to their randomized treatment sequence (generic/RLNAD/generic/RLNAD or RLNAD/generic/RLNAD/generic).

Measurements and Observations: The plasma concentrations of firocoxib 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 as a randomized, masked four-period, two-sequence, two-treatment, single-dose, fully replicated crossover design using 24 horses with a 28-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.

The mixed reference-scaled average bioequivalence approach (RSABE) was used to evaluate bioequivalence. Prior to the analysis, C_{MAX} and AUC values were natural logarithm transformed. The estimated within-subject standard deviation (s_{WR}) of the RLNAD was calculated separately for transformed C_{MAX} and AUC to select the appropriate analysis approach based on FDA Guidances.

- The s_{WR} was less than 0.294 for AUC, so the average bioequivalence method was used to evaluate bioequivalence. The statistical model included fixed effects of treatment, sequence and period, and a random effect of subject nested within sequence. Period was modeled as a repeated factor. Bioequivalence was established because the back-transformed estimated upper and lower bounds of the pertinent 90% confidence interval for geometric mean ratios (generic:RLNAD) were contained within the acceptance limits of 0.80 to 1.25. The analysis results are presented in Table 1.
- The s_{WR} was greater than 0.294 for C_{MAX} , so the RSABE method was used and bioequivalence was established based on the following two criteria:
 - The estimated 95% upper confidence bound for $(\mu_T - \mu_R)^2 - \theta * \sigma_{WR}^2$ is less than zero (0), where μ_T and μ_R are the population means of the natural log transformed primary variable for the generic article and RLNAD, respectively, σ_{WR} is the population with-in subject standard deviation for the RLNAD, $\theta = (\log(1.25)/\sigma_{wo})^2$, and $\sigma_{wo} = 0.25$.
 - The point estimate of the generic to RLNAD geometric mean ratio is contained within the acceptance limits of 0.80 and 1.25.

The analysis results are presented in Table 2.

Table 1. Bioequivalence Evaluation for AUC and T_{MAX}

Parameter	Generic Mean	RLNAD Mean	Ratio [◇]	Lower 90% CI	Upper 90% CI
AUC (ng/mL)*hour	3545 [†]	3332 [†]	1.06	0.99	1.14
T _{MAX} (hours) (SD) [‡]	4 (2.4) [‡]	2 (1.9) [‡]	NE	NE	NE

[†] Geometric mean

[‡] Arithmetic mean and standard deviation (SD)

[◇] Ratio = Test/Reference

CI = confidence interval

NE = not estimated

Table 2. Bioequivalence Evaluation for C_{MAX}

Parameter	S _{WR} [†]	Generic Mean	RLNAD Mean	Ratio [‡]	Upper 95% Bound [◇]
C _{MAX} (ng/mL)	0.357	110.95 [*]	121.52 [*]	0.91	-0.038

[†] Estimated within-subject standard deviation of the RLNAD

^{*} Geometric mean

[‡] Point estimate of the geometric mean ratio (Test/Reference)

[◇] Estimated 95% upper confidence bound for $(\mu_T - \mu_R)^2 - \theta * \sigma_{WR}^2$

Adverse Reactions:

There were no serious adverse events reported during the study.

Conclusion:

The *in vivo* bioequivalence study demonstrated that the generic 57 mg Firocoxib Tablets for Horses and the RLNAD 57 mg Equioxx[®] (firocoxib) Tablets are bioequivalent in horses.

III. HUMAN FOOD SAFETY

This drug is intended for use in horses. 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.

The product labeling contains the following Warning statement: Do not use in horses intended for human consumption.

IV. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to Firocoxib Tablets for Horses:

Human Warnings: Not for use in humans. Keep this and all medications out of the reach of children. Consult a physician in case of accidental ingestion by humans.

V. AGENCY CONCLUSIONS

The data submitted in support of this ANADA satisfy the requirements of section 512(c)(2) of the Federal Food, Drug, and Cosmetic Act. The data demonstrate that Firocoxib Tablets for Horses, when used according to the label, is safe and effective for the indication listed in Section I.M. above.