Date of Approval: July 8, 2025

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA)

ANADA 200-815

Cefpodoxime Proxetil Tablets

Dogs

Cefpodoxime Proxetil Tablets are indicated for the treatment of skin infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, β hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*.

Sponsored by:

Felix Pharmaceuticals Pvt. Ltd.

Executive Summary

Cefpodoxime Proxetil Tablets are approved for the treatment of skin infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, β hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*. The reference listed new animal drug (RLNAD) is SIMPLICEF® (cefpodoxime proxetil tablets) sponsored by Zoetis Inc. under NADA 141-232.

Bioequivalence

The sponsor conducted one *in vivo* blood-level study in dogs to show that the 100 mg Cefpodoxime Proxetil Tablets are bioequivalent to the 100 mg SIMPLICEF® tablets. No serious adverse events related to administration of the generic product or RLNAD were reported during the study.

The sponsor conducted a comparative *in vitro* dissolution study for the additional product strength. Based on the dissolution data, the 200 mg tablets qualified for a waiver from the requirement to perform a separate *in vivo* bioequivalence study (a biowaiver). FDA granted a biowaiver for this strength.

Conclusions

Based on the data submitted by the sponsor for the approval of Cefpodoxime Proxetil 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 200-815

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

Cefpodoxime Proxetil Tablets

D. Drug Product Established Name

cefpodoxime proxetil tablets

E. Pharmacological Category

Antimicrobial

F. Dosage Form

Tablets

G. Amount of Active Ingredient

100 mg and 200 mg

H. How Supplied

100-count and 250-count bottles for each tablet strength

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

The dose range of Cefpodoxime Proxetil Tablets is 5-10 mg/kg (2.3-4.5 mg/lb) body weight, administered orally, once a day. Cefpodoxime Proxetil Tablets should be

administered once daily for 5-7 days or for 2-3 days beyond the cessation of clinical signs, up to a maximum of 28 days. Treatment of acute infections should not be continued for more than 3-4 days if no response to therapy is seen.

K. Route of Administration

Oral

L. Species/Class

Dogs

M. Indication

Cefpodoxime Proxetil Tablets are indicated for the treatment of skin infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus pseudintermedius*, *Staphylococcus aureus*, *Streptococcus canis* (group G, β hemolytic), *Escherichia coli*, *Pasteurella multocida*, and *Proteus mirabilis*.

N. Reference Listed New Animal Drug

SIMPLICEF®; cefpodoxime proxetil tablets; NADA 141-232; Zoetis Inc.

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 (cefpodoxime proxetil tablets) 100 mg tablets. The RLNAD is available in 100 and 200 mg tablet sizes. The *in vivo* blood-level study was conducted in 40 healthy, fasted dogs. 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 100 mg RLNAD (cefpodoxime proxetil tablets) and the 100 mg generic (cefpodoxime proxetil tablets) by the mixed reference-scaled average bioequivalence approach as described in the Statistical Methods section below. A waiver from the requirement to demonstrate *in vivo* bioequivalence (biowaiver) for the generic 200 mg tablets was requested. Dissolution data was used to demonstrate that the generic 200 mg cefpodoxime proxetil tablets are comparable to the generic 100 mg tablet strength used in the *in vivo* blood-level bioequivalence study. Therefore, a biowaiver for the generic 200 mg (cefpodoxime proxetil tablets) was granted. The study information is summarized below.

A. Blood-level Bioequivalence Study in Dogs

Title: Pivotal Bioequivalence Study of SIMPLICEF® Tablets and a Generic Formulation of Cefpodoxime Proxetil Tablets when Administered Orally to Beagle Dogs under Fasted Conditions. (Study No. CEFC-KC2-9723)

Study Dates: November 7, 2023 to March 27, 2024

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 100 mg Cefpodoxime Proxetil Tablets and the RLNAD 100 mg SIMPLICEF® (cefpodoxime proxetil tablets) in fasted dogs.

Study Animals: Forty intact male beagle dogs from 1 year and 49 days to 3 years and 309 days of age and weighing 10 to 12.5 kg on study day -2.

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

Drug Administration: Each animal received 100 mg of either the generic or RLNAD cefpodoxime proxetil tablets according to their randomized treatment sequence (generic/RLNAD/generic/RLNAD or RLNAD/generic/RLNAD/generic).

Measurements and Observations: The plasma concentrations of cefpodoxime 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 crossover design using 40 dogs with a 7-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 reference-scaled average bioequivalence (RSABE) method was used as appropriate to evaluate bioequivalence through the mixed scaling approach. 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 s_{WR} was equal to or 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 $(\mu_T-\mu_R)^2- \theta*\sigma^2_{WR}$ 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, $\theta = (\log (1.25)/\sigma_{W0})^2$ and $\sigma_{W0} =0.25$.

  - The point estimate of the generic to RLNAD geometric mean ratio is contained within the acceptance limits of 0.80 and 1.25.

Results:

As seen in the table below, C_{MAX} and AUC met the pre-specified criteria for bioequivalence (Table II.1). The mean values of T_{MAX} obtained for the generic article and RLNAD were summarized.

Table II.1. Bioequivalence Evaluation

Parameter	s_{WR}	Generic Mean	RLNAD Mean	Ratio[◊]	95% Upper Bound[$]	90% CI for the Ratio
AUC (µg/mL)*hour	0.2135	110.79[†]	116.77[†]	0.95	NE	(0.88, 1.02)
C_{MAX} (µg/mL)	0.3273	10.61[†]	11.24[†]	0.95	-0.0524	NE
T_{MAX} (hours) (SD)[‡]	NE	2.65 (0.70)[‡]	3.25 (3.39)[‡]	NE	NE	NE

[†] Geometric mean
[‡] Arithmetic mean and standard deviation (SD)
[◊] Ratio = Generic/RLNAD
[$] 95% upper confidence bound for $(\mu_T-\mu_R)^2- \theta*\sigma^2_{WR}$
CI = confidence interval
NE = not estimated

Adverse Reactions:

There were no serious adverse events related to administration of the generic product or RLNAD reported during the study.

Conclusion:

The *in vivo* bioequivalence study demonstrated that the generic 100 mg Cefpodoxime Proxetil Tablets and the RLNAD 100 mg SIMPLICEF® (cefpodoxime proxetil tablets) are bioequivalent in dogs.

B. Bioequivalence Waiver

A pivotal *in vivo* blood-level bioequivalence study was conducted using the 100 mg (cefpodoxime proxetil tablets) strength. A waiver from the requirement to perform an *in vivo* bioequivalence study (biowaiver) for the generic 200 mg tablets was requested. To qualify for a biowaiver for this product strength, a comparative *in vitro* dissolution study was conducted to determine the dissolution profiles of the generic and RLNAD 100 mg and 200 mg (cefpodoxime proxetil tablets). Comparisons were made between the following tablets:

- Generic 100 mg and generic 200 mg tablets
- Generic 100 mg and RLNAD 100 mg tablets

The objective was to satisfy f_2 criteria between the generic 100 mg tablet strength and the generic 200 mg tablet strength.

Test conditions were as follows:

- Dissolution apparatus: USP Apparatus II
- Dissolution medium: Phosphate buffer, pH 3.0
- Dissolution medium volume: 900 mL
- Temperature: 37 ± 0.5°C
- Paddle speed: 75 rpm
- Number of vessels: 12
- Data points: 10, 15, 20, 30, 45, and 60 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.

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 200 mg cefpodoxime proxetil tablets is granted.

III. HUMAN FOOD SAFETY

This drug is intended for use in dogs. 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 Cefpodoxime Proxetil Tablets:

Not for human use. Keep this and all drugs out of reach of children. Antimicrobial drugs, including penicillins and cephalosporins, can cause allergic reactions in sensitized individuals. To minimize the possibility of allergic reactions, those handling such antimicrobials, including cefpodoxime, are advised to avoid direct contact of the product with the skin and mucous membranes.

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 Cefpodoxime Proxetil Tablets, when used according to the label, are safe and effective for the conditions of use in the General Information Section above.