Date of Approval: January 29, 2026

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA)

ANADA 200-761

Cronoquin™ Tablets

(marbofloxacin)

Dogs and cats

Cronoquin™ Tablets (marbofloxacin) are indicated for the treatment of infections in dogs and cats associated with bacteria susceptible to marbofloxacin.

Sponsored by:

Cronus Pharma Specialities India Private Ltd.

Executive Summary

Cronoquin™ Tablets (marbofloxacin) are approved for the treatment of infections in dogs and cats associated with bacteria susceptible to marbofloxacin. The reference listed new animal drug (RLNAD) is Zeniquin® (marbofloxacin) tablets sponsored by Zoetis Inc. under NADA 141-151.

Bioequivalence

The sponsor conducted one *in vivo* blood-level study in cats to show that the 25 mg Cronoquin™ Tablets are bioequivalent to the 25 mg Zeniquin® tablets. No serious adverse events were reported during the study. The sponsor also conducted one *in vivo* blood-level study in dogs to show that the 50 mg Cronoquin™ Tablets are bioequivalent to the 50 mg Zeniquin® 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 generic 25 mg, 100 mg, and 200 mg tablets qualified for a waiver from the requirement to perform separate *in vivo* bioequivalence studies (a biowaiver) in dogs. The Food and Drug Administration (FDA) granted a biowaiver for these strengths. Only the 25 mg strength is labeled for use in cats.

Conclusions

Based on the data submitted by the sponsor for the approval of Cronoquin™ Tablets, the 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 200-761

B. Sponsor

Cronus Pharma Specialities India Private Ltd.
Plot No.9(B), Survey No. 99/1, GMR Hyderabad Aviation SEZ Ltd.
Mamidipalle Village, Balapur Mandal, Shamshabad, Rangareddy
Hyderabad, Telangana, 500108, India

Drug Labeler Code: 069043

U.S. Agent Name and Address:

Jodi Beaudry, MS
J^2 Consulting LLC
45 Bugling Elk Ln
Columbus, MT 59019

C. Proprietary Name

Cronoquin™ Tablets

D. Drug Product Established Name

marbofloxacin

E. Pharmacological Category

Antimicrobial

F. Dosage Form

Tablets

G. Amount of Active Ingredient

25 mg, 50 mg, 100 mg, or 200 mg marbofloxacin per tablet

H. How Supplied

25 mg tablets supplied in bottles containing 100 tablets or 250 tablets
50 mg tablets supplied in a bottle containing 100 tablets
100 mg tablets supplied in a bottle containing 50 tablets
200 mg tablets supplied in a bottle containing 50 tablets

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

The recommended dosage for oral administration to dogs and cats is 1.25 mg marbofloxacin per lb of body weight once daily, but the dosage may be safely increased to 2.5 mg/lb.

For the treatment of skin and soft tissue infections, Cronoquin™ Tablets should be given for 2-3 days beyond the cessation of clinical signs for a maximum of 30 days. For the treatment of urinary tract infections, Cronoquin™ Tablets should be administered for at least 10 days. If no improvement is noted within 5 days, the diagnosis should be re-evaluated and a different course of therapy considered.

K. Route of Administration

Oral

L. Species

Dogs and cats

M. Indications

Cronoquin™ Tablets (marbofloxacin) are indicated for the treatment of infections in dogs and cats associated with bacteria susceptible to marbofloxacin.

N. Reference Listed New Animal Drug

Zeniquin®; marbofloxacin; NADA 141-151; 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, two *in vivo* blood-level studies were conducted to demonstrate product bioequivalence using the generic and RLNAD marbofloxacin 25 mg tablets in cats and the 50 mg tablets in dogs. The RLNAD is available in 25 mg, 50 mg, 100 mg, and 200 mg tablet sizes. Only the 25 mg size is labeled for use in cats. One *in vivo* blood-level study was conducted in 24 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 25 mg Zeniquin® tablets and the 25 mg marbofloxacin tablets by the average bioequivalence approach as described in the Statistical Methods section below. One *in vivo* blood-level study was conducted in 30 healthy, fasted dogs. The pivotal parameters to

evaluate bioequivalence are C_{MAX} and AUC from time 0 to the last sampling time before the first unquantifiable concentration after C_{MAX}. Bioequivalence was demonstrated between the 50 mg Zeniquin® tablets and the 50 mg marbofloxacin tablets by the 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 25 mg, 100 mg, and 200 mg tablets in dogs was requested. Dissolution data was used to demonstrate that the generic 100 mg and 200 mg marbofloxacin tablets are comparable to the generic 50 mg tablet strength used in the *in vivo* blood-level bioequivalence study in dogs, and the generic 25 mg tablet strength is comparable to the RLNAD 25 mg tablet strength used in the *in vivo* blood-level bioequivalence study in cats. Therefore, a biowaiver for the generic 25 mg, 100 mg, and 200 mg marbofloxacin tablets in dogs was granted. The study information is summarized below.

A. Blood-level Bioequivalence Study in Cats

Title: Pivotal Bioequivalence Study of Zeniquin® and Generic Marbofloxacin Tablets when Administered Orally to Cats. (Study No. 108-BF-1919)

Study Dates: February 4, 2020, to October 21, 2020

Study Locations:

In-life phase: Ontario, Canada

Bioanalytical testing: Andhra Pradesh, India

Study Design:

Objective: The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence data for the generic 25 mg Cronoquin™ Tablets (marbofloxacin) tablets and the RLNAD 25 mg Zeniquin® (marbofloxacin) tablets in fasted cats.

Study Animals: Twenty-four domestic shorthair cats.

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 25 mg of either the generic or RLNAD marbofloxacin tablets according to their randomized treatment sequence (generic/RLNAD or RLNAD/generic).

Measurements and Observations: The plasma concentrations of marbofloxacin 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, two-period, two-sequence, two-treatment, single-dose crossover design using 24 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	47547.90†	46532.48†	1.02	0.96	1.08
C_{MAX} (ng/mL)	3612.68†	3504.63†	1.03	0.97	1.09
T_{MAX} (hours) (SD)‡	1.47 (0.72)‡	1.67 (0.89)‡	NE	NE	NE

RLNAD = Zeniquin® (marbofloxacin) 25 mg tablet
Generic = generic marbofloxacin 25 mg tablet
† Geometric mean
‡ Arithmetic mean and standard deviation (SD)
◊ Ratio = Test/Reference
CI = confidence interval
NE = not estimated

Adverse Reactions:

There were no serious adverse events related to the test or reference article reported during the study.

Conclusion:

The *in vivo* bioequivalence study demonstrated that the generic 25 mg Cronoquin™ Tablets (marbofloxacin) and the RLNAD 25 mg Zeniquin® (marbofloxacin) tablets are bioequivalent in cats.

B. Blood-level Bioequivalence Study in Dogs

Title: Pivotal Bioequivalence Study of Zeniquin® and Generic Marbofloxacin Tablets when Administered Orally to Dogs. (Study No. TH1180073)

Study Dates: June 27, 2019, to August 5, 2020

Study Locations:

In-life phase: Terre Haute, IN

Bioanalytical testing: Andhra Pradesh, India

Study Design:

Objective: The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence data for the generic 50 mg Cronoquin™ Tablets (marbofloxacin) and the RLNAD 50 mg Zeniquin® (marbofloxacin) tablets in fasted dogs.

Study Animals: Thirty beagle dogs.

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 50 mg of either the generic or RLNAD marbofloxacin tablets according to their randomized treatment sequence (generic/RLNAD or RLNAD/generic).

Measurements and Observations: The plasma concentrations of marbofloxacin 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, two-period, two-sequence, two-treatment, single-dose crossover design using 30 dogs 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.2). The mean values of T_{MAX} obtained for the generic article and RLNAD were summarized.

Table II.2. Bioequivalence Evaluation

Parameter	Generic Mean	RLNAD Mean	Ratio◊	Lower 90% CI	Upper 90% CI
AUC (ng/mL)*hour	26272.33†	26205.60†	1.00	0.96	1.04
C_{MAX} (ng/mL)	2755.39†	2724.50†	1.01	0.99	1.03
T_{MAX} (hours) (SD)‡	1.48 (0.59)‡	1.46 (0.53)‡	NE	NE	NE

RLNAD = Zeniquin® (marbofloxacin) 50 mg tablet
Generic = generic marbofloxacin 50 mg tablet
† Geometric mean
‡ Arithmetic mean and standard deviation (SD)
◊ Ratio = Test/Reference
CI = confidence interval
NE = not estimated

Adverse Reactions:

There were no serious adverse events related to the test or reference article reported during the study.

Conclusion:

The *in vivo* bioequivalence study demonstrated that the generic 50 mg Cronoquin™ Tablets (marbofloxacin) and the RLNAD 50 mg Zeniquin® (marbofloxacin) tablets are bioequivalent in dogs.

C. Bioequivalence Waiver

Two pivotal *in vivo* blood-level bioequivalence studies were conducted using the 25 mg marbofloxacin tablet strength in cats and the 50 mg marbofloxacin tablet strength in dogs. A waiver from the requirement to perform *in vivo* bioequivalence studies (biowaiver) for the generic 25 mg, 100 mg, and 200 mg tablet in dogs 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 25 mg, 50 mg, 100 mg, and 200 mg marbofloxacin tablets, and the RLNAD 25 mg and 50 mg marbofloxacin tablets. The similarity factor (f_2) calculation was used to evaluate dissolution profile comparisons. Comparisons were made between the following tablets:

- Generic 50 mg and generic 25 mg tablets
- Generic 50 mg and generic 100 mg tablets
- Generic 50 mg and generic 200 mg tablets
- Generic 50 mg and RLNAD 50 mg tablets
- RLNAD 25 mg and generic 25 mg tablets
- RLNAD 25 mg and RLNAD 50 mg tablets

The objective was to satisfy f_2 criteria between the generic 50 mg tablet strength and the generic 25 mg, 100 mg, and 200 mg tablet strengths, or between the generic 25 mg tablet strength and the RLNAD 25 mg tablet strength.

Test conditions were as follows:

- Dissolution apparatus: USP Apparatus I (Basket) #20 mesh
- Dissolution medium: Phosphate buffer, pH 7.50±0.05
- Dissolution medium volume: 900 mL
- Temperature: 37±0.5°C
- Paddle speed: 100 rpm
- Number of vessels: 12
- Data points: 10, 15, 20, 30, 45, and 60 minutes

The generic and RLNAD drug lots used in the *in vivo* bioequivalence studies were 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., 10 and 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 f_2 should be greater than 50 to ensure sameness or equivalence of two profiles.

CVM estimated f_2 metrics based on mean data, and a summary of the results is presented in table II.3. below:

Table II.3. Similarity Results

Dissolution Comparison	Similarity Results
50 mg generic to the 25 mg generic	48
50 mg RLNAD to the 25 mg RLNAD	43
50 mg generic to the 100 mg generic	65
50 mg generic to the 200 mg generic	57
50 mg generic to the 50 mg RLNAD	59
25 mg RLNAD to the 25 mg generic	81

Study results demonstrate similar dissolution profiles for two within-product comparisons (generic 50 mg tablet strength to generic 100 mg and 200 mg tablet strengths). The 50 mg generic tablet strength compared to the 25 mg generic tablet strength did not meet the f_2>50 criterion, and so the 50 mg RLNAD tablet strength was compared to the 25 mg RLNAD tablet strength. Since the 50 mg RLNAD tablet strength compared to the 25 mg RLNAD tablet strength also did not meet the f_2>50 criterion, the sponsor was able to compare the 25 mg generic tablet strength to the 25 mg RLNAD tablet strength, which met the f_2>50 criterion. Additionally, the *in vivo* study in cats demonstrated that the 25 mg tablets were bioequivalent, and the *in vivo* study in dogs demonstrated that the 50 mg tablets were bioequivalent. Therefore, a biowaiver for the generic 25 mg, 100 mg, and 200 mg marbofloxacin tablets in dogs is granted.

III. HUMAN FOOD SAFETY

This drug is intended for use in dogs and cats. Because this new animal drug is not intended for use in food-producing animals, FDA 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 Cronoquin™ Tablets:

For use in animals only. Keep out of reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. In case of dermal contact, wash skin with soap and water. Consult a physician if irritation persists following ocular or dermal exposure. Individuals with a history of hypersensitivity to fluoroquinolones should avoid this product. In humans, there is a risk of user photosensitization within a few hours after excessive exposure to quinolones. If excessive accidental exposure occurs, avoid direct sunlight.

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