Date of Approval: December 9, 2013

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-320

ONSIOR tablets

Robenacoxib

Cats

Supplemental approval for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration, in cats ≥ 5.5 lbs (2.5 kg) and ≥ 4 months of age; for up to a maximum of 3 days. This supplement provides for lowering the age limit to ≥ 4 months of age.

Sponsored by:

Novartis Animal Health US, Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 141-320

B. Sponsor

Novartis Animal Health US, Inc.
3200 Northline Ave, suite 300
Greensboro, North Carolina 27408

Drug Labeler Code: 058198

C. Proprietary Name

ONSIOR tablets

D. Established Name

robenacoxib

E. Pharmacological Category

Non-steroidal anti-inflammatory drug (NSAID)

F. Dosage Form:

Non-scored tablet

G. Amount of Active Ingredient

Each tablet contains 6 mg robenacoxib

H. How Supplied

ONSIOR tablets are available as 6 mg round, flavored tablets in blisters. Each individual blister card contains 3 tablets. Ten blister cards are supplied in a carton. Each blister card should be dispensed in an ONSIOR dispensing envelope containing the product insert/information for owner sheet, supplied with the product.

I. Dispensing Status

Rx

J. Dosage Regimen

The dose of ONSIOR (robenacoxib) tablets is 0.45 mg/lb (1 mg/kg) orally once daily, for a maximum of three days.
Preoperatively: Administer dose approximately 30 minutes prior to surgery, at the same time as the pre-anesthetic agents are given.
Postoperatively: Tablets may be given with or without food. See dosing chart for dosage directions.
Dosing Directions: To be used in cats ≥ 5.5 lbs and ≥ 4 months of age. Tablets are not scored and should not be broken.

Table 1: Dosing Table

Body Weight	6 mg ONSIOR (robenacoxib) Tablet
5.5 to 13.2 lbs (2.5 to 6 kg)	1 whole tablet once daily
13.3 to 26.4 lbs (6.1 to 12 kg)	2 whole tablets once daily

Do not use in cats weighing less than 5.5 lbs, as cats less than 5.5 lbs cannot be accurately dosed.

K. Route of Administration

Oral

L. Species/Class

Cats

M. Indication

ONSIOR tablets are indicated for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration, in cats $\geq$ 5.5 lbs (2.5 kg) and $\geq$ 4 months of age; for up to a maximum of 3 days.

N. Effect of Supplement

This supplement provides for lowering the age limit to $\geq$ 4 months of age. All cats should still meet the minimum weight requirement of 5.5 lbs (2.5 kg).

II. EFFECTIVENESS

A. Dosage Characterization

This supplemental approval does not change the previously approved dose. Please refer to the FOI Summary for the original approval of NADA 141-320, dated March 8, 2011, for the ONSIOR tablets dosage characterization.

B. Substantial Evidence

This supplemental approval does not affect effectiveness. Please refer to the FOI Summary for the original approval of NADA 141-320, dated March 8, 2011, for the effectiveness information for ONSIOR tablets.

III. TARGET ANIMAL SAFETY:

A. Interchangeable Use Target Animal Safety Study in 4 Month Old Cats

1. Type of Study: Laboratory safety study

2. Study Location: MPI Research, Inc.
Mattawan, MI

3. General Design

a. Purpose: To evaluate the safety of the interchangeable use of robenacoxib when administered orally to 4-month-old cats using the 6 mg tablets and the 20 mg/mL injection at 1X, 2X, and 3X doses.

b. Test Animals: Four month old, healthy male and female domestic shorthair (DSH) cats were used in the study. The ONSIOR tablet/injectable treatment groups had 4 cats/sex and the control group had 5 cats/sex.

c. Control: Empty gelatin capsules were used as the oral control and saline for injection, at a volume equivalent to the 3X dose group, was used as the subcutaneous control.

d. Dosage form: ONSIOR tablets (6 mg per tablet) and robenacoxib 20 mg/mL in solution for injection (ONSIOR injectable)

e. Route of administration: Tablets were administered orally and subcutaneous injections were administered over the scapular area using different sites during the course of the study.

f. Study duration: Thirty-seven days

g. Dosages used: Oral and subcutaneous treatments were alternated over a 37-day period according to a schedule of 7 days tablet then 3 days subcutaneous injection, 7 days tablet/3 days subcutaneous injection, 7 days tablet/3 days subcutaneous injection, then 7 days tablet. Cats were dosed at 1X, 2X, and 3X the upper limit of the inherent dose band (tablets), and the injectable point dose. The 1X dose is 2 mg/kg subcutaneously for the injection. The 1X dose for the tablet is based on the maximum exposure of 2.4 mg/kg (the actual mg/kg dose received depended upon the cat's weight due to the inherent dose band of the non-scored, one-size, 6 mg tablet). One additional group served as the negative control and received the control articles at the 3X dose level.

Table 2: Treatment Groups for the Interchangeable Use Study

Group	Dose	Number and Sex of Animals
1	Saline or empty gelatin capsules (0 mg/kg)	5 M / 5 F
2	1X (2.4 mg/kg oral & 2 mg/kg injectable)	4 M / 4 F
3	2X (4.8 mg/kg oral & 4 mg/kg injectable)	4 M / 4 F
4	3X (7.2 mg/kg oral & 6.0 mg/kg injectable)	4 M / 4 F

h. Variables measured: The following variables were measured prior to study initiation, during, and/or at the end of the study – body weight, food consumption, clinical observations and injection site evaluations, physical, ophthalmic, electrocardiographic and neurological examinations, body

temperature, coagulation and buccal mucosal bleeding times (BMBT), hematology and clinical chemistries, urinalyses, organ weights, and gross pathology and histopathology. Blood samples were also collected for periodic pharmacokinetic analysis.

4. Results: All cats survived to termination of study.

   a. Clinical observations: One 2X cat vomited twice during the last 2 dosing days of the study. Soft stools were noted sporadically in all groups, including the controls, during the treatment period. However, soft stools were seen more frequently in the higher dose groups.

   b. Injection sites: There was a dose dependent increase in the incidence of injection site edema. There was a greater incidence of injection site edema at 8 hours post-injection in 2X cats and a greater incidence of injection site edema at 24 and 48 hours post-injection in 3X cats compared to the control group. Injection site edema generally resolved within 48 hours except for one 2X cat and one 3X cat where edema was observed up to 120 hours post-injection.

   c. Electrocardiography: There was a dose dependent increase in the QT interval at all 3 dose levels that was statistically significantly different from control group values following treatment. In addition, a longer PR interval was noted in 1X group females on Day 36 as compared to the controls. The significance of the increased QT interval in cats is unknown.

   d. Hematology and clinical chemistry evaluations: One 2X cat had an approximately seven-fold increase in the BMBT (217 seconds) compared to the pre-treatment value. All other coagulation values for this cat remained within reference ranges. Both treated and control cats had elevated creatinine kinase (CK) levels. The highest elevations were seen in female treated cats during the study.

   e. Pathology and organ weights: There was dose dependent, minimal to mild subacute/chronic inflammation of the subcutaneous tissue at injection sites in the 2X and 3X groups. Two treated cats were noted to have decreased myeloid:erythroid ratios (M:E). One 1X cat had mild, transient anemia and a moderately decreased M:E ratio with a moderate increase in lymphoid cells at the end of the study. One 2X cat had a mild decrease in M:E ratio with a moderate decrease in lymphoid cells. Histologically, one 1X cat had a minimal ulcer on the tongue, and one 3X cat had focal minimal mineralization of the left ventricular papillary muscle.

5. Conclusions: Under the conditions of this study, 4 month old cats administered 3 cycles of 7 days of oral robenacoxib tablets followed by 3 days of robenacoxib injections, and a final course of 7 days of tablets remained clinically in good health over this 37 day study. There was a dose dependent increase in QT intervals at all three doses. This study supports the safety of ONSIOR tablets for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration for a maximum of 3 days in cats $\geq$4 months of age and $\geq$ 5.5 lbs.

IV. HUMAN FOOD SAFETY:

This drug is intended for use in cats which are non-food animals. 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 NADA.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to ONSIOR tablets (robenacoxib):

> Human Warnings are provided on the product label as follows: "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 use in cats only."

VI. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR part 514. The data demonstrate that ONSIOR (robenacoxib) tablets, when used according to the label, are safe and effective for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration in cats $\geq$ 5.5 lbs (2.5 kg) and $\geq$ 4 months of age; for up to a maximum of 3 days.

A. Marketing Status:

The drug is restricted to use by or on the order of, a licensed veterinarian because professional expertise is needed to diagnose and provide guidance in the control of postoperative pain. Furthermore, the veterinarian monitors patients for possible adverse effects of the drug.

B. Exclusivity:

This supplemental approval for ONSIOR (robenacoxib) tablets qualifies for THREE years of marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act because the supplemental approval included a safety study. This exclusivity begins as of the date of our approval letter and only applies to the new lower age limit of $\geq$ 4 months (changed from $\geq$ 6 months to $\geq$ 4 months of age) that is approved in the supplemental application.

C. Supplemental Application:

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(2)).

D. Patent Information:

For current information on patents, see the Animal Drugs @ FDA database or the Green Book on the FDA CVM internet website.