Date of Approval: November 23, 2011

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-203

DERAMAXX Chewable Tablets
Dogs

The effect of the supplement is the addition of a new indication for the control of postoperative pain and inflammation associated with dental surgery in dogs at a dose of 0.45-0.91 mg/lb (1-2 mg/kg) administered orally once daily for 3 days.

Sponsored by:

Novartis Animal Health US, Inc.

TABLE OF CONTENTS

I. GENERAL INFORMATION:

A. File Number:	NADA 141-203
B. Sponsor:	Novartis Animal Health US, Inc. 3200 Northline Ave. Suite 300 Greensboro, NC 27408 Drug Labeler Code: 058198
C. Proprietary Name:	DERAMAXX Chewable Tablets
D. Established Name:	Deracoxib
E. Pharmacological Category:	Non-steroidal anti-inflammatory drug (NSAID)
F. Dosage Form:	Chewable Tablet
G. Amount of Active Ingredient:	12 mg, 25 mg, 50 mg, 75 mg, and 100 mg
H. How Supplied:	Round, brownish, half-scored tablets in 7, 30, and 90 count bottles
I. How Dispensed:	Rx
J. Dosages:	The daily dose of DERAMAXX tablets for the control of pain and inflammation associated with osteoarthritis in dogs is 0.45-0.91 mg/lb/day (1-2 mg/kg/day) as a single daily dose, as needed. The dose for postoperative dental pain is 0.45-0.91 mg/lb/day (1-2 mg/kg/day) as a single daily dose for 3 days. The first dose should be given approximately 1 hour prior to dental surgery and subsequent doses should be given daily for up to two additional treatments. The dose for postoperative orthopedic pain is 1.4-1.8 mg/lb/day (3-4 mg/kg/day) as a single daily dose, as needed, not to exceed 7 days of administration. Tablets are scored and dosage should be calculated in half-tablet increments.
K. Route of Administration:	Oral

A. File Number:	NADA 141-203
L. Species/Class:	Dogs
M. Indications:	For the control of pain and inflammation associated with osteoarthritis in dogs, and for the control of postoperative pain and inflammation associated with orthopedic surgery and dental surgery in dogs.
N. Effect of Supplement:	This supplement provides for the addition of a new indication for the control of postoperative pain and inflammation associated with dental surgery in dogs at a dose of 0.45-0.91 mg/lb (1-2 mg/kg) administered orally once daily for 3 days.

II. EFFECTIVENESS:

A. Dosage Characterization:

This supplemental approval does not change the dosage of 0.45-0.91 mg/lb (1-2 mg/kg) administered orally once daily that is approved for the control of pain and inflammation associated with osteoarthritis in dogs. A dose of 1.4-1.8 mg/lb (3-4 mg/kg) administered orally once daily is approved for the control of postoperative pain and inflammation associated with orthopedic surgery in dogs. The lower dose of 0.45-0.91 mg/lb (1-2 mg/kg) was chosen based on clinical experience and the effectiveness of the lower dose for treating osteoarthritis. The Freedom of Information (FOI) Summary for the original approval of NADA 141-203, dated February 11, 2003, contains the dosage characterization information for the 0.45-0.91 mg/lb (1-2 mg/kg) oral, once daily dose of DERAMAXX Chewable Tablets as needed for the control of pain and inflammation associated with osteoarthritis.

B. Substantial Evidence:

(1) Field Study

(a) Type of Study: Placebo-controlled, masked, randomized field study

(b) Investigators:

Larry Baker, DVM
Decatur, IL

Roger Sifferman, DVM
Springfield, MO

Amy Jessup, DVM
Winston-Salem, NC

Philip VanVranken, DVM
Battle Creek, MI

(c) General Design:

1 Purpose: The objective of this study was to evaluate the effectiveness and safety of DERAMAXX tablets at a dose of 0.45-0.91 mg/lb (1-2 mg/kg) administered orally once daily for 3 days for the control of pain and inflammation associated with dental surgery in dogs.

2 Test animals: Sixty-two client-owned dogs presented for dental extractions were enrolled in the study at 4 locations. Male and female dogs, representing various breeds and ranging from 1.5-16 years in age and 6.3-49.4 kg body weight, were included. There were 31 dogs enrolled in both the DERAMAXX and placebo treatment groups.

3 Pre-medications: All animals received butorphanol administered as a pre-anesthetic medication.

4 Control: The placebo was a commercially available pet vitamin tablet.

5 Dosage form: DERAMAXX® Chewable Tablets (market formulation)

6 Route of administration: Oral

7 Dosage: 0.45-0.91 mg/lb (1-2 mg/kg) administered once daily. The first treatment was given at least 1 hour prior to dental surgery before any pre-anesthetics were administered. Dogs received up to two additional daily treatments. For consistency, the additional treatments were administered at approximately the same time each day.

8 Test duration: 3 days

9 Parameters measured: DERAMAXX was compared to the placebo control group on a success/failure basis after dental extractions of one or more canine, maxillary 4th premolar, maxillary 1st molar, and mandibular 1st molar teeth according to acceptable veterinary dental practice. Extractions included the creation of a gingival flap, sectioning of the tooth as necessary, removal of bone, and closure of the surgical site. Treatment failure was defined as the need for administration of rescue therapy to control post surgical pain. Pain assessors used a modification of the Glasgow Composite Pain Scale (mGCPS) to assess pain.[1] A dog was rescued if it scored ≥ 4 on the combined mGCPS variables of Posture/Activity, Demeanor, Response to Touch, and Vocalization, or if the investigator determined at any time that pain intervention was needed. Any pain intervention constituted a treatment failure. Eating was assessed as a separate variable.

Clinical pathology samples were collected and baseline mGCPS scores were determined prior to test article administration on the day of surgery. Scheduled evaluations for mGCPS scoring were conducted approximately 90 min, 3 h, 5 h and 8 h after extubation on the day of surgery (Day 0).

[1] Holton, L., Reid, J., Scott, E.M., Pawson, P. and Nolan, A. (2001). Development of a behaviour-based scale to measure acute pain in dogs. Veterinary Record, 148, 525-531.

Additional evaluations occurred approximately 2 h and 8 h after test article administration the day after surgery (Day 1), and again approximately 2 h after test article administration the second day after surgery (Day 2). However, pain intervention therapy could be administered at any time at the discretion of the investigator. Once pain intervention was determined to be needed, pain intervention therapy was administered, clinical pathology samples were collected, an exit physical examination was completed, body weight was determined, and the dog was removed from the study. Dogs removed from the study prior to completion on Day 2 were monitored for an additional 24 h and any abnormal observations were recorded.

(d) Statistical Analysis: The primary efficacy variable was 'Rescue' and was analyzed using a generalized linear mixed model. Superiority was established when there was a statistically significant difference and numerical reduction in the proportion of rescues in the DERAMAXX treated group compared to the placebo control group. Total mGCPS scores were calculated as the sum of the Posture/Activity, Demeanor, Response to Touch, and Vocalization scores. Change in body weight was analyzed using a mixed model analysis of variance. Clinical pathology variables were analyzed using a mixed model analysis of covariance. Only statistically significant results are reported.

(e) Results: Fifty-seven dogs were included in the effectiveness evaluations whereas all 62 dogs enrolled in the study were included in the safety assessment. Twenty out of 30 (66.67%) placebo control dogs were rescued during the study (treatment failures) compared to 4 out of 27 (14.81%) DERAMAXX treated dogs requiring rescue therapy. The difference in treatment success/failure outcomes was statistically significant (p=0.0338) in favor of the DERAMAXX treated group. Success/failure results are summarized in Table 1.

Table 1. Treatment Outcomes

Treatment	Outcome* Success	Outcome* Failure	Total
DERAMAXX	23 (85.19%)	4 (14.81%)	27
Placebo Control	10 (33.33%)	20 (66.67%)	30
Total	33	24	57

*The difference in proportion of rescues was statistically significant (p=0.0338).

(f) Adverse reactions: A total of 62 male and female dogs of various breeds, 1.5-16 years old, were included in the field safety analysis. Table 2 shows the number of dogs displaying each adverse reaction. Digestive tract disorders (diarrhea and vomiting) and systemic disorders (abnormal clinical chemistry results) were the most frequently reported findings. There were no distinct breed, age, or sex predilections for adverse reactions that were reported. No dogs were withdrawn from the study due to the occurrence of an adverse reaction.

Table 2. Adverse Reactions in the Dental Pain Field Study[1]

Clinical Observation	DERAMAXX n= 31	Placebo n= 31
Vomiting	4	1
Diarrhea/Soft Stool	3	1
Regurgitation	0	2
Increased AST[2]	3	0
Increased ALT[2]	1	0
Hematuria	1	0
Leukocytosis	1	1
Neutrophilia	1	1
Lameness	1	0
Facial Swelling	0	1
Tachycardia	0	1

[1]Dogs may have experienced more than one of the observations during the study.
[2]Included animals with results over 2x the high normal.

(g) Conclusions: DERAMAXX Chewable Tablets, when administered orally at a dose of 0.45-0.91 mg/lb (1-2 mg/kg) body weight once 1 hour prior to dental surgery and continuing once a day for two days, was effective for the control of postoperative pain and inflammation associated with dental surgery.

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this supplemental approval. The FOI Summary for the original approval of NADA 141-203 dated August 21, 2002, for the postoperative pain indication contains a summary of target animal safety studies for dogs.

IV. HUMAN FOOD SAFETY:

This drug is intended for use in dogs, 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 DERAMAXX Chewable Tablets:

> "Not for use in humans. Keep this and all medication out of reach of children. Consult a physician in case of accidental ingestion by humans."

The following items were examined to ensure human user safety: the Material Safety Data Sheets (MSDS) for deracoxib, the FOI Summaries for DERAMAXX (NADA 141-203), and the Drug Experience Reports submitted to FDA regarding this NADA.

VI. AGENCY CONCLUSIONS:

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514. The data demonstrate that DERAMAXX Chewable Tablets, when used according to the label, are safe and effective for the control of postoperative pain and inflammation associated with dental surgery in dogs.

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 dental postoperative pain and monitor the safe use of the product.

B. Exclusivity:

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for three years of marketing exclusivity beginning on the date of the approval. The three years of marketing exclusivity applies only to the postoperative dental pain indication for which this supplement is approved.

C. Supplemental Applications:

This supplemental NADA did not require a reevaluation of the safety 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 (formerly the Green Book) on the FDA CVM internet website.