

Date of Approval: APR 27 2005

**FREEDOM OF INFORMATION SUMMARY**  
**ORIGINAL NEW ANIMAL DRUG APPLICATION (ANADA)**

ANADA 200-366

Carprofen Caplets  
(carprofen)

25 mg, 75 mg, and 100 mg caplets

Dogs

For the relief of pain and inflammation associated with osteoarthritis

Sponsored by:

IMPAX Laboratories, Inc.

2005-200-366

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## FREEDOM OF INFORMATION SUMMARY

### ***1. GENERAL INFORMATION:***

- a. File Number: ANADA 200-366
- b. Sponsor: IMPAX Laboratories, Inc.  
30831 Huntwood Ave.  
Hayward, CA 94544  
  
Drug Labeler Code: 000115
- c. Established Name: Carprofen
- d. Proprietary Name: Carprofen Caplets
- e. Dosage Form: Scored caplet
- f. How Supplied: 25 mg caplets: Bottles of 60, 100, and 180  
  
75 mg and 100 mg caplets: Bottles of 60 and 180
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: 25 mg, 75 mg, or 100 mg carprofen per caplet
- i. Route of Administration: Oral
- j. Species/Class: Dogs
- k. Recommended Dosage: The total daily dose may be administered as 2 mg/lb (4.4 mg/kg) of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) of body weight twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.
- l. Pharmacological Category: Anti-inflammatory/Analgesic
- m. Indications: For the relief of pain and inflammation associated with osteoarthritis in dogs.
- n. Pioneer Product: RIMADYL Caplets; carprofen; NADA 141-053; Pfizer, Inc.

## **2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:**

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

### **A. Blood-level Bioequivalence Study**

One blood-level bioequivalence study was conducted to determine the comparative bioavailability of the generic and pioneer formulations of carprofen caplets.

**Protocol Title:** A Randomized, Two-Way Crossover, Single-Dose, Open-Label Study to Evaluate the Relative Bioavailability of a Test Tablet Formulation of Carprofen (25 mg) Compared to an Equivalent Dose of a Commercially Available Reference Drug (RIMADYL Caplets, 25 mg, Pfizer, Inc.) in 36 Fasted, Healthy Dogs

**Testing Facility:** Southwest Bio-Labs, Inc.  
401 North 17<sup>th</sup> St., Suite 11  
Las Cruces, NM

**Study Number:** Southwest Bio-Labs, Inc.: 202-0624d

**Objective:** The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence of IMPAX Laboratories, Inc.'s 25 mg carprofen caplets and Pfizer, Inc.'s RIMADYL Caplets, 25 mg, in a 2 way crossover study in dogs.

**Summary:** Thirty-six beagle dogs (18 males (M) and 18 females (F)) were randomly assigned to two treatment groups containing 18 animals (9M + 9F). Each group was given an oral dose of 25 mg of carprofen of either the IMPAX formulation or the Pfizer RIMADYL formulation in a 2-way crossover study. The dogs ranged in age from 1 to 4 years and weighed  $22 \pm 6$  pounds. Phase I began on Study Day one with Group I animals receiving the IMPAX formulation and Group II animals receiving the Pfizer formulation. After a 7 day washout, Phase II began on Study Day 8 with the Group I animals receiving the Pfizer formulation and the Group 2 receiving the IMPAX formulation. For each phase of the study, pre-dose blood samples were taken and sampling continued with post-dose samples taken at 0.25, 0.50, 0.75, 1, 1.5, 2, 4, 6, 12, 24, 36, and 48 hours. All blood samples collected were processed, plasma harvested, and stored frozen until shipped to PHARMout Laboratories, Inc., Sunnyvale, CA for carprofen analysis using a fully validated analytical method.

**Results:** The following pharmacokinetic (PK) parameters were computed from the plasma concentration data using the actual sample collection times:

- $AUC_{0-LOQ}$ : Area under the plasma concentration-time curve (ng-hr/mL) from time zero to the time of the last quantifiable concentration (t), calculated using the linear trapezoidal rule:

$$\sum_i (t_i - t_{i-1})(C_i + C_{i-1})/2, i=1 \text{ to } t, \text{ where } C_i \text{ is the plasma concentration at time } t_i.$$

- $C_{max}$ : Maximum or peak concentration obtained by inspection (ng/mL).
- $T_{max}$ : Time of maximum or peak concentration, obtained by inspection (hr).

The calculated values of  $C_{max}$ ,  $AUC_{0-LOQ}$ , and  $T_{max}$  for the test and reference products are represented in the table below.

PK Parameter	Carprofen Mean	Rimadyl Mean	% Ratio	90% Confidence Interval (expressed as a percentage)
$C_{max}$	31341.75*	30501.72*	102.75	-3.81, 9.77
$AUC_{0-LOQ}$	179879.32*	183880.22*	97.82	-8.75, 4.87
$T_{max}$	1.11**	1.12**	99.11	NA

\*Geometric means listed are based on back transformed least squares means of ln-transformed values.

\*\*Least square means are calculated from non-transformed data.

The criteria for calculating the confidence bounds for the PK parameters of interest, as described in CVM's Bioequivalence Guidance, is to construct a 90% confidence interval about the difference of the two means, generic minus pioneer, based on the log scale of each parameter and then take the anti-log of the confidence limits minus 1 multiplied by 100. The resulting bounds should be between -20.00% and +25.00% of the mean of the reference product. As seen in the table, the two pivotal pharmacokinetic parameters for determining product bioequivalence,  $AUC_{0-LOQ}$  and  $C_{max}$ , fall within those bounds.

The PK parameter,  $T_{max}$ , is interpreted by clinical judgment and the difference is not medically important. Therefore, the study objective to determine the bioequivalence of generic and pioneer carprofen products was achieved.

### B. Dissolution Study

*In vitro* dissolution data were submitted in support of the request for waiver of *in vivo* bioequivalence study requirements for the 75 mg and 100 mg strength caplets. The *in vitro* dissolution data were generated in accordance with CVM's requests (900 mL freshly degassed phosphate buffer, pH 7.5, using Apparatus 2 at 50 rpm). The sponsor also provided information confirming that the inactive ingredients for the IMPAX product do not interfere with the UV spectrophotometric methods used for quantitating the amount of carprofen dissolved in the dissolution buffer (absorbance at 300 nm, tested against the standard solution).

To demonstrate comparable *in vitro* dissolution between the proposed IMPAX and RIMADYL products, the following criteria were required:

- 1) Twelve units of the test and reference products are used for each set of dissolution tests.
- 2) The relative standard deviation in percent dissolved less than 15% at the first sampling time and equal to or less than 10% at all other sampling times.
- 3) Comparability is based upon the model-free approach as defined in CDER's 8/97 guidance for industry titled "Dissolution Testing of Immediate Release Dosage Forms". The similarity factor ( $f_2$ ) is calculated as follows:

$$f_2 = 50 * \log \left\{ \left[ 1 + \frac{1}{n} \sum_{t=1}^n (R_t - T_t)^2 \right]^{-0.5} * 100 \right\}$$

where n = the number of time points,  $R_t$  is the mean dissolution value of the reference product at time t, and  $T_t$  is the mean dissolution value of the test product at time t. Comparability is defined by  $f_2$  values are equal to or greater than 50.

The *in vitro* dissolution data demonstrated that in each dissolution comparison the relative standard deviation was less than 10%. Thus, the  $f_2$  criterion could be employed for comparing profiles.

A requirement for conducting the dissolution study was that if the 25 mg test and reference products were bioequivalent but presented with very different *in vitro* dissolution profiles, then the 75 mg and 100 mg test products could be compared to the lot of the 25 mg strength IMPAX product that underwent *in vivo* bioequivalence testing. The 25 mg IMPAX and RIMADYL caplets presented with markedly different *in vitro* profiles. Nevertheless, these two products were shown to be bioequivalent. Accordingly, the 75 mg and 100 mg strength IMPAX caplets were compared to the lot of the 25 mg IMPAX caplet that underwent *in vitro* testing. IMPAX conducted two sets of dissolution runs on the 25 mg caplets: one to cover the request for waiver of the 75 mg caplets and a second to cover the waiver request for the 100 mg caplets.

Calculations of  $f_2$  using means based upon the exact percent dissolved reported for each caplet are presented in the table below.

Comparability of 25 mg to 75 mg and 100mg Carprofen Caplets  
 Similarity Factor ( $f_2$ ) calculations

Comparison	$f_2$
75 vs. 25	49.2
100 vs. 25	48.9

CVM concluded that slight deviations from 50 do not necessarily indicate that the two curves are different. In particular, considering that the very marked *in vitro* differences observed between the 25 mg strengths of RIMADYL and IMPAX caplets did not influence product performance, we have, with confidence, concluded that the very slight deviation between the 25 mg versus 75 mg and 100 mg caplet profiles will have no impact on *in vivo* product performance. Accordingly, a waiver of *in vivo* bioequivalence study requirements for 75 mg and 100 mg strength caplets was granted.

**3. HUMAN 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, data on human safety pertaining to drug residues in food were not required for approval of this ANADA.

**4. AGENCY CONCLUSIONS:**

This Abbreviated New Animal Drug Application (ANADA) filed under section 512(b)(2) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that Carprofen Caplets, when used under its proposed conditions of use, is safe and effective for its labeled indications.

**5. ATTACHMENTS:**

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-366: Carprofen Caplets  
Container labels for 25 mg caplets in bottles of 60, 100, and 180  
Container labels for 75 mg and 100 mg caplets in bottles of 60 and 180  
Package Insert  
Dog Owner Information Summary

Pioneer Labeling for NADA 141-053: RIMADYL Caplets  
Container labels for 25 mg, 75 mg, and 100 mg caplets in bottles of 14, 60 and 180, and blister packs containing 4 caplets  
Package Insert  
Dog Owner Information Summary



**GLOBAL**

NDC 0115-3311-13

### Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**25 mg**

**60 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 25 mg of carprofen. Indications: Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

Dosage: The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please refer to insert for complete Warnings and Precautions.

Store at controlled room temperature, 15°-30°C (59°-86°F).

Mfg. by: IMPAX Laboratories, Inc.  
Hayward, CA 94544 USA  
Global Pharmaceuticals  
Division of IMPAX Laboratories, Inc.  
Philadelphia, PA 19124 USA

Rev. 12/04  
312-01

Bar Code  
0115-3311-13

Lot No.:

Exp. Date



**GLOBAL**

NDC 0115-3311-01

### Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**25 mg**

**100 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 25 mg of carprofen. Indications: Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

Dosage: The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

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0115-3311-01

Lot No.:

Exp. Date



**GLOBAL**

NDC 0115-3311-19

### Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**25 mg**

**180 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 25 mg of carprofen. Indications: Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

Dosage: The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

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Store at controlled room temperature, 15°-30°C (59°-86°F).

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417-01

Bar Code  
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Lot No.:

Exp. Date



**GLOBAL**<sup>®</sup>

NDC 0115-3322-13

## Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

**Caution:** Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**75 mg**

**60 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 75 mg of carprofen. **Indications:** Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

**Dosage:** The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

**Warnings:** Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. **For use in dogs only. Do not use in cats. Please refer to insert for complete Warnings and Precautions.**

Store at controlled room temperature, 15°-30°C (59°-86°F).

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Hayward, CA 94544 USA

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Bar Code  
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NDC 0115-3322-19

## Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

**Caution:** Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**75 mg**

**180 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 75 mg of carprofen. **Indications:** Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

**Dosage:** The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

**Warnings:** Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. **For use in dogs only. Do not use in cats. Please refer to insert for complete Warnings and Precautions.**

Store at controlled room temperature, 15°-30°C (59°-86°F).

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Philadelphia, PA 19124 USA

Rev. 12/04  
338-01

Bar Code  
0115-3322-19

Lot No.:

Exp. Date



NDC 0115-3333-13

### Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**100 mg**

**60 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 100 mg of carprofen. Indications: Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

Dosage: The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please refer to insert for complete Warnings and Precautions.

Store at controlled room temperature, 15°-30°C (59°-86°F).

Mfg. by: IMPAX Laboratories, Inc.  
Hayward, CA 94544 USA

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Division of IMPAX Laboratories, Inc.  
Philadelphia, PA 19124 USA

Rev. 12/04  
330-01

Bar Code  
0115-3333-13

Lot No.:

Exp. Date



NDC 0115-3333-19

### Carprofen Caplets

*Non-steroidal  
anti-inflammatory drug*

**For oral use in dogs only**

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**100 mg**

**180 Caplets**

ANADA #200-366, Approved by FDA

Each scored caplet contains 100 mg of carprofen. Indications: Carprofen is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

Dosage: The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-caplet increments.

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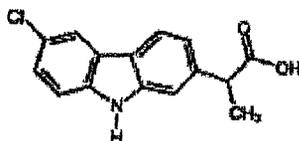
Lot No.:

Exp. Date

## Carprofen Caplets, 25 mg, 75 mg and 100 mg

For oral use in dogs only

*Non-steroidal anti-inflammatory drug*



### CAUTION

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

### DESCRIPTION

Carprofen is a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class that includes ibuprofen, naproxen, and ketoprofen. The chemical name for carprofen, a substituted carbazole, is 6-chloro-alpha-methyl-9H-carbazole-2-acetic acid. The empirical formula is  $C_{15}H_{12}ClNO_2$  and the molecular weight 273.72. The chemical structure of carprofen is shown above. Carprofen is a white, crystalline compound. It is freely soluble in ethanol, but practically insoluble in water at 25°C.

### CLINICAL PHARMACOLOGY

Carprofen is a non-narcotic, non-steroidal anti-inflammatory agent with characteristic analgesic and antipyretic activity approximately equipotent to indomethacin in animal models.<sup>1</sup>

The mechanism of action of carprofen, like that of other NSAIDs, is believed to be associated with the inhibition of cyclooxygenase activity. Two unique cyclooxygenases have been described in mammals.<sup>2</sup> The constitutive cyclooxygenase, COX-1, synthesizes prostaglandins necessary for normal gastrointestinal and renal function. The inducible cyclooxygenase, COX-2, generates prostaglandins involved in inflammation. Inhibition of COX-1 is thought to be associated with gastrointestinal and renal toxicity while inhibition of COX-2 provides anti-inflammatory activity. The specificity of a particular NSAID for COX-2 versus COX-1 may vary from species to species.<sup>3</sup> In an in vitro study using canine cell cultures, carprofen demonstrated selective inhibition of COX-2 versus COX-1.<sup>4</sup> Clinical relevance of these data has not been shown. Carprofen has also been shown to inhibit the release of several prostaglandins in two inflammatory cell systems: rat polymorphonuclear leukocytes (PMN) and human rheumatoid synovial cells, indicating inhibition of acute (PMN system) and chronic (synovial cell system) inflammatory reactions.<sup>1</sup>

Several studies have demonstrated that carprofen has modulatory effects on both humoral and cellular immune responses.<sup>5-9</sup> Data also indicate that carprofen inhibits the production of osteoclast-activating factor (OAF),  $PGE_1$ , and  $PGE_2$  by its inhibitory effect in prostaglandin biosynthesis.<sup>1</sup>

Based upon comparison with data obtained from intravenous administration, carprofen is rapidly and nearly completely absorbed (more than 90% bioavailable) when administered orally.<sup>10</sup> Peak blood plasma concentrations are achieved in 1-3 hours after oral administration of 1, 5, and 25 mg/kg to dogs. The mean terminal half-life of carprofen is approximately 8 hours (range 4.5-9.8 hours) after single oral doses varying

from 1–35 mg/kg of body weight. After a 100 mg single intravenous bolus dose, the mean elimination half-life was approximately 11.7 hours in the dog. Carprofen is more than 99% bound to plasma protein and exhibits a very small volume of distribution.

Comparison of a single 25 mg dose in Beagle dogs after subcutaneous and oral administration demonstrated that the dorsoscapular subcutaneous administration results in a slower rate of drug input (as reflected by mean peak observed concentrations) but comparable total drug absorption within a 12 hour dosing interval (as reflected by area under the curve from hours zero to 12 postdose).

Carprofen is eliminated in the dog primarily by biotransformation in the liver followed by rapid excretion of the resulting metabolites (the ester glucuronide of carprofen and the ether glucuronides of 2 phenolic metabolites, 7-hydroxy carprofen and 8-hydroxy carprofen) in the feces (70–80%) and urine (10–20%). Some enterohepatic circulation of the drug is observed.

### **INDICATIONS**

Carprofen Caplets are indicated for the relief of pain and inflammation associated with osteoarthritis in dogs.

### **DOSAGE AND ADMINISTRATION**

Always provide Client Information Sheet with prescription. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. Carprofen Caplets are scored and dosage should be calculated in half-tablet increments. Tablets can be halved by placing the tablet on a hard surface and pressing down on both sides of the score. Carprofen Caplets should be given by mouth and may be given with or without food. Care should be taken to ensure that the dog consumes the complete dose.

### **EFFECTIVENESS**

Confirmation of the effectiveness of carprofen for the relief of pain and inflammation associated with osteoarthritis was demonstrated in 7 placebo-controlled, masked studies examining the anti-inflammatory and analgesic effectiveness of carprofen in various breeds of dogs.

Separate placebo-controlled, masked, multicenter field studies confirmed the anti-inflammatory and analgesic effectiveness of carprofen when dosed at 2 mg/lb once daily or when divided and administered at 1 mg/lb twice daily. In these 2 field studies, dogs diagnosed with osteoarthritis showed statistically significant overall improvement based on lameness evaluations by the veterinarian and owner observations when administered carprofen at labeled doses.

### **ANIMAL SAFETY STUDIES**

Laboratory studies in unanesthetized dogs and clinical field studies have demonstrated that carprofen is well tolerated in dogs after oral administration.

In target animal safety studies, carprofen was administered orally to healthy Beagle dogs at 1, 3, and 5 mg/lb twice daily (1, 3 and 5 times the recommended total daily dose) for 42 consecutive days with no significant adverse reactions. Serum albumin for a single female dog receiving 5 mg/lb twice daily decreased to 2.1 g/dL after 2 weeks of

treatment, returned to the pre-treatment value (2.6 g/dL) after 4 weeks of treatment, and was 2.3 g/dL at the final 6-week evaluation. Over the 6-week treatment period, black or bloody stools were observed in 1 dog (1 incident) treated with 1 mg/lb twice daily and in 1 dog (2 incidents) treated with 3 mg/lb twice daily. Redness of the colonic mucosa was observed in 1 male that received 3 mg/lb twice daily.

Two of 8 dogs receiving 10 mg/lb orally twice daily (10 times the recommended total daily dose) for 14 days exhibited hypoalbuminemia. The mean albumin level in the dogs receiving this dose was lower (2.38 g/dL) than each of 2 placebo control groups (2.88 and 2.93 g/dL, respectively). Three incidents of black or bloody stool were observed in 1 dog. Five of 8 dogs exhibited reddened areas of duodenal mucosa on gross pathologic examination. Histologic exam of these areas revealed no evidence of ulceration, but did show minimal congestion of the lamina propria in 2 of the 5 dogs.

In separate safety studies lasting 13 and 52 weeks, respectively, dogs were administered orally up to 11.4 mg/lb/day (5.7 times the recommended total daily dose of 2 mg/lb) of carprofen. In both studies, the drug was well tolerated clinically by all of the animals. No gross or histologic changes were seen in any of the treated animals. In both studies, dogs receiving the highest doses had average increases in serum L-alanine aminotransferase (ALT) of approximately 20 IU.

In the 52-week study, minor dermatologic changes occurred in dogs in each of the treatment groups but not in the control dogs. The changes were described as slight redness or rash and were diagnosed as non-specific dermatitis. The possibility exists that these mild lesions were treatment related, but no dose relationship was observed.

Clinical field studies were conducted with 549 dogs of different breeds at the recommended oral doses for 14 days (297 dogs were included in a study evaluating 1 mg/lb twice daily and 252 dogs were included in a separate study evaluating 2 mg/lb once daily). In both studies the drug was clinically well tolerated and the incidence of clinical adverse reactions for carprofen-treated animals was no higher than placebo-treated animals (placebo contained inactive ingredients found in carprofen caplets). For animals receiving 1 mg/lb twice daily, the mean post-treatment serum ALT values were 11 IU greater and 9 IU less than pre-treatment values for dogs receiving carprofen caplets and placebo, respectively. Differences were not statistically significant. For animals receiving 2 mg/lb once daily, the mean post-treatment serum ALT values were 4.5 IU greater and 0.9 IU less than pre-treatment values for dogs receiving carprofen caplets and placebo, respectively. In the latter study, 3 carprofen-treated dogs developed a 3-fold or greater increase in (ALT) and/or (AST) during the course of therapy. One placebo-treated dog had a greater than 2-fold increase in ALT. None of these animals showed clinical signs associated with laboratory value changes. Changes in the clinical laboratory values (hematology and clinical chemistry) were not considered clinically significant. The 1 mg/lb twice daily course of therapy was repeated as needed at 2-week intervals in 244 dogs, some for as long as 5 years.

Carprofen was well tolerated when used in conjunction with a variety of anesthetic-related drugs. The type and severity of abnormal health observation in carprofen- and placebo-treated animals were approximately equal and few in number (see Adverse Reactions). The most frequent abnormal health observation was vomiting and was observed at approximately the same frequency in carprofen- and placebo-treated animals. Changes in clinicopathologic indices of hematopoetic, renal, hepatic, and

clotting function were not clinically significant. The mean post-treatment serum ALT values were 7.3 IU and 2.5 IU less than pre-treatment values for dogs receiving carprofen caplets and placebo, respectively. The mean post-treatment AST values were 3.1 IU less for dogs receiving carprofen and 0.2 IU greater for dogs receiving placebo.

### **CONTRAINDICATIONS**

Carprofen should not be used in dogs exhibiting previous hypersensitivity to carprofen.

### **PRECAUTIONS**

As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal and renal toxicity. Effects may result from decreased prostaglandin production and inhibition of the enzyme cyclooxygenase which is responsible for the formation of prostaglandins from arachidonic acid.<sup>11-14</sup> When NSAIDs inhibit prostaglandins that cause inflammation they may also inhibit those prostaglandins which maintain normal homeostatic function. These anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease more often than in healthy patients.<sup>12,14</sup> NSAID therapy could unmask occult disease which has previously been undiagnosed due to the absence of apparent clinical signs. Patients with underlying renal disease for example, may experience exacerbation or decompensation of their renal disease while on NSAID therapy.<sup>11-14</sup> The use of parenteral fluids during surgery should be considered to reduce the potential risk of renal complications when using NSAIDs perioperatively.

Carprofen is an NSAID, and as with others in that class, adverse reactions may occur with its use. The most frequently reported effects have been gastrointestinal signs. Events involving suspected renal, hematologic, neurologic, dermatologic, and hepatic effects have also been reported. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be approached cautiously, with appropriate monitoring. Since many NSAIDs possess the potential to induce gastrointestinal ulceration, concomitant use of carprofen with other anti-inflammatory drugs, such as corticosteroids and NSAIDs, should be avoided or very closely monitored. Sensitivity to drug-associated adverse reactions varies with the individual patient. For example, carprofen treatment was not associated with renal toxicity or gastrointestinal ulceration in well-controlled safety studies of up to ten times the dose in dogs.

Carprofen is not recommended for use in dogs with bleeding disorders (e.g., Von Willebrand's disease), as safety has not been established in dogs with these disorders. The safe use of carprofen in animals less than 6 weeks of age, in pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. Safety has not been established for IV or IM administration. Studies to determine the activity of carprofen when administered concomitantly with other protein-bound or similarly metabolized drugs have not been conducted. Drug compatibility should be monitored closely in patients requiring additional therapy. Such drugs commonly used include cardiac, anticonvulsant and behavioral medications. It has been suggested that treatment with carprofen may reduce the level of inhalant anesthetics needed.<sup>15</sup> It is suggested to use different sites for additional injections. If additional pain medication is warranted after administration of the total daily dose of carprofen, alternative analgesia should be considered. The use of another NSAID is not recommended.

Carprofen Caplets should be stored out of reach of dogs in a secured location. Severe adverse reactions may occur if large quantities of caplets are ingested. If you suspect your dog has consumed Carprofen Caplets above the labeled dose, please call your veterinarian for immediate assistance and notify IMPAX Laboratories, Inc. at 1-800-296-5227.

#### **INFORMATION FOR DOG OWNERS**

Carprofen, like other drugs of its class, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include decreased appetite, vomiting, diarrhea, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes.

**Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue carprofen therapy and contact their veterinarian immediately if signs of intolerance are observed.**

The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized, the drug is withdrawn, and veterinary care, if appropriate, is initiated. Owners should be advised of the importance of periodic follow up for all dogs during administration of any NSAID.

#### **WARNINGS**

Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats.

All dogs should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests to establish hematological and serum biochemical baseline data prior to, and periodically during, administration of any NSAID should be considered. **Owners should be advised to observe for signs of potential drug toxicity (see Information for Dog Owners and Adverse Reactions).**

#### **ADVERSE REACTIONS**

During investigational studies with an oral carprofen formulation at twice daily administration of 1 mg/lb, no clinically significant adverse reactions were reported. Some clinical signs were observed during field studies (n=297) which were similar for carprofen caplet- and placebo-treated dogs. Incidences of the following were observed in both groups: vomiting (4%), diarrhea (4%), changes in appetite (3%), lethargy (1.4%), behavioral changes (1%), and constipation (0.3%). The product vehicle served as control.

There were no serious adverse events reported during clinical field studies with once daily administration of 2 mg/lb. The following categories of abnormal health observations were reported. The product vehicle served as control.

**Percentage of Dogs with Abnormal Health Observations Reported  
in Clinical Field Study (2 mg/lb once daily)**

<b>Observation</b>	<b>carprofen caplet (n= 129)</b>	<b>Placebo (n=132)</b>
Inappetence	1.6	1.5
Vomiting	3.1	3.8
Diarrhea/Soft stool	3.1	4.5
Behavior change	0.8	0.8
Dermatitis	0.8	0.8
PU/PD	0.8	-
SAP increase	7.8	8.3
ALT increase	5.4	4.5
AST increase	2.3	0.8
BUN increase	3.1	1.5
Bilirubinuria	16.3	12.1
Ketonuria	14.7	9.1

Clinical pathology parameters listed represent reports of increases from pre-treatment values; medical judgment is necessary to determine clinical relevance.

## **Post-Approval Experience**

Although not all adverse reactions are reported, the following adverse reactions are based on voluntary post-approval adverse drug experience reporting. The categories of adverse reactions are listed in decreasing order of frequency by body system.

**Gastrointestinal:** *Vomiting, diarrhea, constipation, inappetence, melena, hematemesis, gastrointestinal ulceration, gastrointestinal bleeding, pancreatitis.*

**Hepatic:** *Inappetence, vomiting, jaundice, acute hepatic toxicity, hepatic enzyme elevation, abnormal liver function test(s), hyperbilirubinemia, bilirubinuria, hypoalbuminemia. Approximately one-fourth of hepatic reports were in Labrador Retrievers.*

**Neurologic:** *Ataxia, paresis, paralysis, seizures, vestibular signs, disorientation.*

**Urinary:** *Hematuria, polyuria, polydipsia, urinary incontinence, urinary tract infection, azotemia, acute renal failure, tubular abnormalities including acute tubular necrosis, renal tubular acidosis, glucosuria.*

**Behavioral:** *Sedation, lethargy, hyperactivity, restlessness, aggressiveness.*

**Hematologic:** *Immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, blood loss anemia, epistaxis.*

**Dermatologic:** *Pruritus, increased shedding, alopecia, pyotraumatic moist dermatitis (hot spots), necrotizing panniculitis/vasculitis, ventral ecchymosis.*

**Immunologic or hypersensitivity:** *Facial swelling, hives, erythema.*

In rare situations, death has been associated with some of the adverse reactions listed above.

To report a suspected adverse reaction call 1-800-296-5227.

## STORAGE

Store tablets at controlled room temperature 15°–30°C (59°–86°F).

## HOW SUPPLIED

Carprofen Caplets 25 mg—Each light orange, convex tablet debossed with “G” on one side and bisected on the other side with “33” on the left and “11” on the right of the bisect.

Bottles of 60..... NDC 0115-3311-13  
Bottles of 100..... NDC 0115-3311-01  
Bottles of 180..... NDC 0115-3311-19

Carprofen Caplets 75 mg—Each light orange, convex tablet debossed with “G” on one side and bisected on the other side with “33” on the left and “22” on the right of the bisect.

Bottles of 60..... NDC 0115-3322-13  
Bottles of 180..... NDC 0115-3322-19

Carprofen Caplets 100 mg—Each light orange, convex tablet debossed with “G” on one side and bisected on the other side with “33” on the left and “33” on the right of the bisect.

Bottles of 60..... NDC 0115-3333-13  
Bottles of 180..... NDC 0115-3333-19

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To report a suspected adverse reaction call IMPAX Laboratories, Inc. at 1-800-296-5227.

ANADA #200-366, Approved by FDA

Mfg. by:  
IMPAX Laboratories, Inc.  
Hayward, CA 94544

Dist. by:  
Global Pharmaceuticals  
Division of IMPAX Laboratories, Inc.  
Philadelphia, PA 19124

Rev 12/2004  
316-00

## **Dog Owner Information about Carprofen Caplets for Osteoarthritis Pain**

This summary contains important information about Carprofen Caplets. You should read this information before you start giving your dog Carprofen Caplets and review it each time the prescription is refilled. This sheet is provided only as a summary and does not take the place of instructions from your veterinarian. Talk to your veterinarian if you do not understand any of this information or if you want to know more about Carprofen Caplets.

### **What is Carprofen Caplets?**

Carprofen Caplets are a nonsteroidal anti-inflammatory drug (NSAID) that is used to reduce pain and inflammation (soreness) due to osteoarthritis in dogs. A licensed veterinarian must prescribe carprofen for your dog. It is available as a caplet and is given to dogs by mouth.

Osteoarthritis (OA) is a painful condition caused by "wear and tear" of cartilage and other parts of the joints that may result in the following changes or signs in your dog:

- Limping or lameness
- Decreased activity or exercise (reluctance to stand, climb stairs, jump or run, or difficulty in performing these activities)
- Stiffness or decreased movement of joints

### **What kind of results can I expect when my dog is on Carprofen Caplets for OA?**

While Carprofen Caplets are not a cure for osteoarthritis, it can relieve the pain and inflammation of OA and improve your dog's mobility.

- Response varies from dog to dog but can be quite dramatic.
- In most dogs, improvement can be seen in a matter of days.
- If Carprofen Caplets are discontinued or not given as directed, your dog's pain and inflammation may come back.

### **Who should not take Carprofen Caplets?**

Your dog should not be given Carprofen Caplets if he/she:

- Has had an allergic reaction to the active ingredient, carprofen.
- Has had an allergic reaction to aspirin or other NSAIDs (for example etodolac or phenylbutazone) such as hives, facial swelling, or red or itchy skin.

**Carprofen Caplets should be given to dogs only.** Cats should not be given Carprofen Caplets. Call your veterinarian immediately if your cat receives Carprofen Caplets. People should not take Carprofen Caplets. Keep Carprofen Caplets and all medicines out of reach of children. Call your physician immediately if you accidentally take Carprofen Caplets.

### **How to give Carprofen Caplets to your dog.**

Carprofen Caplets should be given according to your veterinarian's instructions. Your veterinarian will tell you what amount of Carprofen Caplets is right for your dog and for how long it should be given. Carprofen Caplets should be given by mouth and may be given with or without food.

### **What to tell/ask your veterinarian before giving Carprofen Caplets.**

Talk to your veterinarian about:

- The signs of OA you have observed (for example limping, stiffness).
- The importance of weight control and exercise in the management of OA.
- What tests might be done before Carprofen Caplets is prescribed.
- How often your dog may need to be examined by your veterinarian.
- The risks and benefits of using Carprofen Caplets.

Tell your veterinarian if your dog has ever had the following medical problems:

- Experienced side effects from Carprofen Caplets or other NSAIDs, such as aspirin
- Digestive upset (vomiting and/or diarrhea)
- Liver disease
- Kidney disease
- A bleeding disorder (for example, Von Willebrand's disease)

Tell your veterinarian about:

- Any other medical problems or allergies that your dog has now or has had.
- All medicines that you are giving your dog or plan to give your dog, including those you can get without a prescription.

Tell your veterinarian if your dog is:

- Pregnant, nursing or if you plan to breed your dog.

### **What are the possible side effects that may occur in my dog during Carprofen Caplets therapy?**

Carprofen, like other drugs, may cause some side effects. Serious but rare side effects have been reported in dogs taking NSAIDs, including Carprofen Caplets. Serious side effects can occur with or without warning and in rare situations result in death.

The most common NSAID-related side effects generally involve the stomach (such as bleeding ulcers), and liver or kidney problems. Look for the following side effects that can indicate your dog may be having a problem with Carprofen Caplets or may have another medical problem:

- Decrease or increase in appetite
- Vomiting
- Change in bowel movements (such as diarrhea, or black, tarry or bloody stools)
- Change in behavior (such as decreased or increased activity level, incoordination, seizure or aggression)
- Yellowing of gums, skin, or whites of the eyes (jaundice)
- Change in drinking habits (frequency, amount consumed)
- Change in urination habits (frequency, color, or smell)
- Change in skin (redness, scabs, or scratching)

It is important to stop therapy and contact your veterinarian immediately if you think your dog has a medical problem or side effect from Carprofen Caplets therapy. If you have additional questions about possible side effects, talk to your veterinarian.

### **Can Carprofen Caplets be given with other medicines?**

Carprofen Caplets should not be given with other NSAIDs (for example, aspirin, etodolac) or steroids (for example, cortisone, prednisone, dexamethasone, triamcinolone).

Tell your veterinarian about all medicines you have given your dog in the past, and any medicines that you are planning to give with Carprofen Caplets. This should include other medicines that you can get without a prescription. Your veterinarian may want to check that all of your dog's medicines can be given together.

### **What do I do in case my dog eats more than the prescribed amount of Carprofen Caplets?**

Contact your veterinarian immediately if your dog eats more than the prescribed amount of Carprofen Caplets.

### **What else should I know about Carprofen Caplets?**

This page provides a summary of information about Carprofen Caplets. If you have any questions or concerns about Carprofen Caplets or osteoarthritis pain, talk to your veterinarian.

As with all prescribed medicines, Carprofen Caplets should only be given to the dog for which it was prescribed. It should be given to your dog only for the condition for which it was prescribed.

It is important to periodically discuss your dog's response to Carprofen Caplets at regular check ups. Your veterinarian will best determine if your dog is responding as expected and if your dog should continue receiving Carprofen Caplets.

To report a suspected adverse reaction call IMPAX Laboratories, Inc. at 1-800-296-5227.

Rev. 12/04

Each scored caplet contains 25 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue surgery. Always consult your veterinarian for the correct use of Rimadyl. See the complete information sheet with prescription. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose should be administered as 1 mg/lb (2.2 mg/kg) twice daily. For the control of postoperative pain, administer approximately 2 hours before the procedure. Caplets are scored and dosage should be calculated in half-caplet increments. © 1997, 85-8500-03 Made in USA

**RIMADYL®**  
(carprofen)  
Caplets  
Non-steroidal anti-inflammatory drug  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

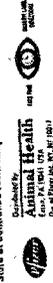
**25 mg**

**60 caplets**

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



Each scored caplet contains 25 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue surgery. Always consult your veterinarian for the correct use of Rimadyl. See the complete information sheet with prescription. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose should be administered as 1 mg/lb (2.2 mg/kg) twice daily. For the control of postoperative pain, administer approximately 2 hours before the procedure. Caplets are scored and dosage should be calculated in half-caplet increments. © 1997, 85-8501-03 Made in USA

**RIMADYL®**  
(carprofen)  
Caplets  
Non-steroidal anti-inflammatory drug  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

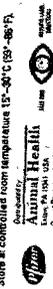
**25 mg**

**180 caplets**

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



Each scored caplet contains 25 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs. Disease: The recommended dosage for oral administration to dogs is 1 mg/lb of body weight twice daily. Caplets are scored and dosage should be calculated in half-caplet increments. © 1997, 85-8500-40 Made in USA

**RIMADYL®** (carprofen)  
Caplets  
Non-steroidal anti-inflammatory drug  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

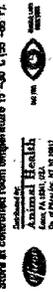
**25 mg**

**14 caplets - For trial use only. Not for sale.**

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



**RIMADYL®**  
(carprofen)

25 mg

4 caplets

For oral use in dogs only

**Caution:** Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Non-steroidal  
anti-inflammatory drug

NADA #141-053, Approved by FDA



**RIMADYL®** (carprofen)



Distributed by:  
Pfizer Animal Health, Exton, PA 19341, USA  
Div. of Pfizer Inc., NY, NY 10017

Lot: 2311469S  
Exp: 03/2006

8568000  
033 20-0293-00

Each scored caplet contains 75 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postsoperative pain associated with soft tissue and orthopedic surgeries in dogs. Dosage: Always provide Client Information Sheet with prescription. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight once daily. Total daily dose may be administered as 1 mg/lb (2.2 mg/kg) twice daily. For the control of postsoperative pain, administer approximately 2 hours before the procedure. Caplets are scored and dosage should be calculated in half-caplet increments.

**RIMADYL®**  
(carprofen)  
Caplets

**Non-steroidal anti-inflammatory drug**  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

75 mg 

60 caplets

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



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**Animal Health**  
Kenilworth, NJ, USA  
Kenilworth, NJ, USA



Made in USA  
027 85-8602-03



Each scored caplet contains 75 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postsoperative pain associated with soft tissue and orthopedic surgeries in dogs. Dosage: Always provide Client Information Sheet with prescription. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. For the control of postsoperative pain, administer approximately 2 hours before the procedure. Caplets are scored and dosage should be calculated in half-caplet increments.

**RIMADYL®**  
(carprofen)  
Caplets

**Non-steroidal anti-inflammatory drug**  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

75 mg 

180 caplets

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



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Made in USA  
027 85-8603-03

Each scored caplet contains 75 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs. Dosage: The recommended dosage for oral administration to dogs is 1 mg/lb of body weight twice daily. Caplets are scored and dosage should be calculated in half-caplet increments.

**RIMADYL® (carprofen)**  
Caplets

**Non-steroidal anti-inflammatory drug**  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

75 mg 

14 caplets - For trial use only. Not for sale.

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



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Kenilworth, NJ, USA  
Kenilworth, NJ, USA



Made in USA  
027 85-8681-00

**RIMADYL®**  
(carprofen)

**75 mg**

**4 caplets**

**For oral use in dogs only**

**Caution:** Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**Non-steroidal  
anti-inflammatory drug**

NADA #141-053, Approved by FDA



**RIMADYL® (carprofen)**



*Distributed by:*  
Pfizer Animal Health, Exton, PA 19341, USA  
Div. of Pfizer Inc., NY, NY 10017

Lot: 2311413S  
Exp: 02/2006

8567000  
033 20-0294-00

Each scored caplet contains 100 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. For the control of postoperative pain, Rimadyl should be administered approximately 2 hours before the procedure. Caplets are scored and dosage should be calculated in half-caplet increments.

**RIMADYL®**  
(carprofen)  
Caplets

**Non-steroidal anti-inflammatory drug**  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

100 mg

60 caplets

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



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Kenilworth, NJ 07033  
Div. of Pfizer Inc., NY, NY 10017



Made in USA  
027 85-8604-03

Each scored caplet contains 100 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs. The recommended dosage for oral administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. For the control of postoperative pain, administer approximately 2 hours before the procedure. Caplets are scored and dosage should be calculated in half-caplet increments.

**RIMADYL®**  
(carprofen)  
Caplets

**Non-steroidal anti-inflammatory drug**  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

100 mg

180 caplets

NADA #141-053, Approved by FDA



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**Animal Health**  
Kenilworth, NJ 07033  
Div. of Pfizer Inc., NY, NY 10017



Made in USA  
027 85-8605-03

**RIMADYL®** (carprofen)  
Caplets  
**Non-steroidal anti-inflammatory drug**  
For oral use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

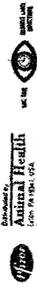
100 mg

14 caplets - For trial use only. Not for sale.

NADA #141-053, Approved by FDA



Warnings: Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. For use in dogs only. Do not use in cats. Please Refer to Insert for Complete Warnings and Precautions. Store at controlled room temperature 15°-30°C (59°-86°F).



Distributed by:  
**Animal Health**  
Kenilworth, NJ 07033  
Div. of Pfizer Inc., NY, NY 10017



Each scored caplet contains 100 mg of carprofen. Indications: Rimadyl is indicated for the relief of pain and inflammation associated with osteoarthritis in dogs. The recommended dosage for oral administration to dogs is 1 mg/lb of body weight twice daily. Caplets are scored and dosage should be calculated in half-caplet increments.

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## Dog Owner Information about RIMADYL® Caplets (carprofen) Rimadyl® (pronounced "Rim-a-dill") for Osteoarthritis and Post-Surgical Pain Generic name: carprofen ("car-prō-fen")

This summary contains important information about Rimadyl. You should read this information before you start giving your dog Rimadyl and review it each time the prescription is refilled. This sheet is provided only as a summary and does not take the place of instructions from your veterinarian. Talk to your veterinarian if you do not understand any of this information or if you want to know more about Rimadyl.

### What is Rimadyl?

Rimadyl is a nonsteroidal anti-inflammatory drug (NSAID) that is used to reduce pain and inflammation (soreness) due to osteoarthritis and pain following surgery in dogs. Rimadyl is a prescription drug for dogs. It is available as a caplet and chewable tablet and is given to dogs by mouth. Osteoarthritis (OA) is a painful condition caused by "wear and tear" of cartilage and other parts of the joints that may result in the following changes or signs in your dog:

- Limping or lameness
- Decreased activity or exercise (reluctance to stand, climb stairs, jump or run, or difficulty in performing these activities)
- Stiffness or decreased movement of joints

To control surgical pain (e.g. for surgeries such as spays, ear procedures or orthopedic repairs) your veterinarian may administer Rimadyl before the procedure and recommend that your dog be treated for several days after going home.

### What kind of results can I expect when my dog is on Rimadyl?

While Rimadyl is not a cure for osteoarthritis, it can relieve the pain and inflammation of OA and improve your dog's mobility

- Response varies from dog to dog but can be quite dramatic.
- In most dogs, improvement can be seen in a matter of days.
- If Rimadyl is discontinued or not given as directed, your dog's pain and inflammation may come back.

### Who should not take Rimadyl?

Your dog should not be given Rimadyl if he/she:

- Has had an allergic reaction to carprofen, the active ingredient of Rimadyl.
- Has had an allergic reaction to aspirin or other NSAIDs (for example etodolac or phenylbutazone) such as hives, facial swelling, or red or itchy skin.

**Rimadyl should be given to dogs only.** Cats should not be given Rimadyl. Call your veterinarian immediately if your cat receives Rimadyl. People should not take Rimadyl. Keep Rimadyl and all medicines out of reach of children. Call your physician immediately if you accidentally take Rimadyl.

### How to give Rimadyl to your dog.

Rimadyl should be given according to your veterinarian's instructions. Your veterinarian will tell you what amount of Rimadyl is right for your dog and for how long it should be given. Rimadyl should be given by mouth and may be given with or without food.

### What to tell/ask your veterinarian before giving Rimadyl.

Talk to your veterinarian about:

- The signs of OA you have observed (for example limping, stiffness).
- The importance of weight control and exercise in the management of OA.
- What tests might be done before Rimadyl is prescribed.
- How often your dog may need to be examined by your veterinarian.
- The risks and benefits of using Rimadyl.

Tell your veterinarian if your dog has ever had the following medical problems:

- Experienced side effects from Rimadyl or other NSAIDs, such as aspirin
- Digestive upset (vomiting and/or diarrhea)
- Liver disease
- Kidney disease
- A bleeding disorder (for example, Von Willebrand's disease)

Tell your veterinarian about:

- Any other medical problems or allergies that your dog has now or has had.
- All medicines that you are giving your dog or plan to give your dog, including those you can get without a prescription.

Tell your veterinarian if your dog is:

- Pregnant, nursing or if you plan to breed your dog.

### What are the possible side effects that may occur in my dog during Rimadyl therapy?

Rimadyl, like other drugs, may cause some side effects. Serious but rare side effects have been reported in dogs taking NSAIDs, including Rimadyl. Serious side effects can occur with or without warning and in rare situations result in death.

The most common NSAID-related side effects generally involve the stomach (such as bleeding ulcers), and liver or kidney problems. Look for the following side effects that can indicate your dog may be having a problem with Rimadyl or may have another medical problem:

- Decrease or increase in appetite
- Vomiting
- Change in bowel movements (such as diarrhea, or black, tarry or bloody stools)
- Change in behavior (such as decreased or increased activity level; incoordination, seizure or aggression)
- Yellowing of gums, skin, or whites of the eyes (jaundice)
- Change in drinking habits (frequency, amount consumed)
- Change in urination habits (frequency, color, or smell)
- Change in skin (redness, scabs, or scratching)

It is important to stop therapy and contact your veterinarian immediately if you think your dog has a medical problem or side effect from Rimadyl therapy. If you have additional questions about possible side effects, talk to your veterinarian.

### Can Rimadyl be given with other medicines?

Rimadyl should not be given with other NSAIDs (for example, aspirin, etodolac) or steroids (for example, cortisone, prednisone, dexamethasone, triamcinolone).

Tell your veterinarian about all medicines you have given your dog in the past, and any medicines that you are planning to give with Rimadyl. This should include other medicines that you can get without a prescription. Your veterinarian may want to check that all of your dog's medicines can be given together.

### What do I do in case my dog eats more than the prescribed amount of Rimadyl?

Contact your veterinarian immediately if your dog eats more than the prescribed amount of Rimadyl.

### What else should I know about Rimadyl?

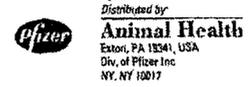
This sheet provides a summary of information about Rimadyl. If you have any questions or concerns about Rimadyl, or osteoarthritis, or postoperative pain, talk to your veterinarian.

As with all prescribed medicines, Rimadyl should only be given to the dog for which it was prescribed. It should be given to your dog only for the condition for which it was prescribed.

It is important to periodically discuss your dog's response to Rimadyl at regular check ups. Your veterinarian will best determine if your dog is responding as expected and if your dog should continue receiving Rimadyl.

To report a suspected adverse reaction call Pfizer Animal Health at 1-800-366-5288.

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