



(302) 934-4049

19 August 2004

Dr. Lonnie Luther, Staff Chief (HFV-102)  
C/O: Dockets Management Branch, HFA-305  
Room 1061  
5630 Fishers Lane  
Food and Drug Administration  
Rockville, MD 20852

**RE: SUITABILITY PETITION FOR REVIEW AND ACTION – CARPROFEN CHEWABLE TABLETS (JINAD 11-188)**

Dear Dr. Luther:

Please find enclosed a suitability petition for Agency review and action. Intervet Inc. is requesting permission to file an abbreviated new animal drug application (ANADA) for a generic carprofen chewable tablet that differs in dosage form from the pioneer product (Rimadyl®; NADA 141-053).

Your timely review of the enclosed petition will be greatly appreciated.

Please feel free to call (302-934-4049) or e-mail ([ruth.lacrosse-vernimb@intervet.com](mailto:ruth.lacrosse-vernimb@intervet.com)) me should you have any questions or if I can be of assistance.

Sincerely,

A handwritten signature in cursive script that reads "Ruth LaCrosse-Vernimb".

Ruth LaCrosse-Vernimb  
Manager, Regulatory Compliance and Quality Assurance – Pharmaceuticals  
Intervet Inc.

Enclosure

2004P-0372

CP 1

**Suitability Petition**

**Intervet Inc.  
Carprofen Chewable Tablet for Dogs  
19 August 2004**

The undersigned submits this petition under Section 512 (n) (3) of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to permit the filing of an abbreviated application for a generic carprofen chewable tablet formulation that differs in dosage form from the pioneer product (Rimadyl<sup>®</sup> NADA 141-053).

**Action Requested**

We are requesting that the Commissioner permit the filing of an abbreviated application for our proposed chewable carprofen tablet for dogs (trade name to be determined). The abbreviated application will include bioequivalence and palatability studies. Our proposed product differs from the pioneer product as follows:

**Pioneer Product****Trade name**

Rimadyl<sup>®</sup> (NADA 141-053)

**Active ingredients**

Carprofen

**Dosage form**

Scored caplets for oral administration

**Strength**

Caplets containing 25 mg, 75 mg, or 100 mg carprofen per caplet

**Sponsor**

Pfizer Animal Health

**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. 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.

**Proposed Drug Product****Trade name**

To be selected.

**Active ingredients**

Carprofen

**Dosage form**

Chewable, single-scored tablets for oral administration

**Strength**

Chewable tablets containing 25 mg, 75 mg, or 100 mg carprofen per tablet

**Sponsor**

Intervet Inc.

**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. For the control of postoperative pain, administer approximately 2 hours before the procedure. The chewable tablets are scored and dosage should be calculated in half-tablet increments.

### **Statement of Grounds**

Chewable tablets of the same strengths as the pioneer product are being developed. The tablet formulation will differ from the pioneer product. The abbreviated application will include bioequivalence studies to demonstrate equivalency of the proposed drug product to the pioneer product and palatability studies to demonstrate the palatability of the chewable tablet formulation.

### **Environmental Impact**

Intervet Inc. requests a categorical exclusion from the requirements to file an environmental impact assessment under 21 CFR 25.33 (d) (1) as the drug is intended for use in nonfood animals.

### **Economic Impact**

Information pertaining to the economic impact of this petition will be submitted if requested by the Commissioner.

### **Differences Between Pioneer and Proposed Drug Product Labeling**

The changes in the labeling noted below may not be placed in the same area as they are located on the pioneer product. The changes noted will be reflected in the proposed drug product's labeling in an appropriate manner so that it is clear and readily understood by the end-user. Please see the attached proposed labeling.

References to Rimadyl<sup>®</sup> will be changed to "carprofen" or to the new brand name as appropriate throughout the labeling.

The Rimadyl<sup>®</sup> name and logo will be removed and replaced with the new brand name and logo throughout the labeling.

References to the caplets will be changed to indicate chewable tablets.

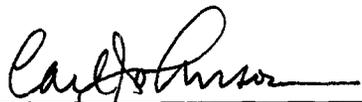
The net weight of the product will be changed to reflect the net weight of the proposed drug product.

The product number will be changed.

The patent number will be removed from the packaging.

**Certification**

Intervet Inc. certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the petition.



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Carl Johnson, AM, DVM  
Director, Product Development and Regulatory  
Affairs – Pharmaceuticals  
Intervet Inc.  
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P.O. Box 318  
Millsboro, DE 19966-0318  
(302) 934-8051

*19 Aug 04*

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Date

Proposed Generic Labeling

**"Trade Name" (to be selected)**  
(carprofen)

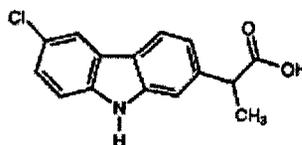
**Chewable Tablets**

***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.

**DESCRIPTION:** "Trade Name" (carprofen) is a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class that includes ibuprofen, naproxen, and ketoprofen. Carprofen is the nonproprietary designation for a substituted carbazole, 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:



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<sub>1</sub>, and PGE<sub>2</sub> by its inhibitory effects on 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.

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:** "Trade Name" 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.

**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. For the control of postoperative pain, administer approximately 2 hours before the procedure. Tablets are scored and dosage should be calculated in half-tablet increments.

**EFFECTIVENESS:** Confirmation of the effectiveness of carprofen for the relief of pain and inflammation associated with osteoarthritis, and for the control of postoperative pain associated with soft tissue and orthopedic surgeries was demonstrated in 5 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 two 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.

Separate placebo-controlled, masked, multicenter field studies confirmed the effectiveness of carprofen for the control of postoperative pain when dosed at 2 mg/lb once daily in various breeds of dogs. In these studies, dogs presented for ovariohysterectomy, cruciate repair and aural surgeries were administered carprofen preoperatively and for a maximum of 3 days (soft tissue) or 4 days (orthopedic) postoperatively. In general, dogs administered carprofen showed statistically significant improvement in pain scores as compared to controls.

**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 stools were observed in 1 dog. Five of 8 dogs exhibited reddened areas of duodenal mucosa on gross pathologic examination. Histologic examination 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). 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 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 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.

Clinical field studies were conducted in 297 dogs of different breeds undergoing orthopedic or soft tissue surgery. Dogs were administered 2 mg/lb of carprofen two hours prior to surgery then once daily, as needed for 2 days (soft tissue surgery) or 3 days (orthopedic surgery). Carprofen was well tolerated when used in conjunction with a variety of anesthetic-related drugs. The type and severity of abnormal health observations 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 hematopoietic, 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 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:** "Trade Name" 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, pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. 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>

If additional pain medication is warranted after the administration of the total daily dose of "Trade Name", alternative analgesia should be considered. The use of another NSAID is not recommended.

**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 of osteoarthritis with 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- 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 of osteoarthritis 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  
Osteoarthritis Field Study (2 mg/lb once daily)**

<b>Observation</b>	<b>Carprofen (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.

During investigational studies of surgical pain with carprofen, no clinically significant adverse reactions were reported. The product vehicle served as control.

**Percentage of Dogs with Abnormal Health Observations Reported in  
Surgical Pain Field Studies with Carprofen (2 mg/lb once daily)**

<b>Observation*</b>	<b>Carprofen (n=148)</b>	<b>Placebo (n=149)</b>
Vomiting	10.1	13.4
Diarrhea/soft stool	6.1	6.0
Ocular disease	2.7	0
Inappetance	1.4	0
Dermatitis/skin lesion	2.0	1.3
Dysrhythmia	0.7	0
Apnea	1.4	0
Oral/periodontal disease	1.4	0
Pyrexia	0.7	1.3
Urinary tract disease	1.4	1.3
Wound drainage	1.4	0

\*A single dog may have experienced more than one occurrence of an event.

**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 1-800-441-8272.

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

**HOW SUPPLIED:** "Trade Name" chewable tablets are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per tablet. Each chewable tablet size is packaged in bottles containing 60 or 180 tablets.

**REFERENCES:**

1. Baruth H, *et al*: In Anti-Inflammatory and Anti-Rheumatic Drugs, Vol. II, Newer Anti-Inflammatory Drugs, Rainsford KD, ed. CRC Press, Boca Raton, pp. 33-47, 1986.
2. Vane JR, Botting RM: Mechanism of action of anti-inflammatory drugs. *Scand J Rheumatol* 25:102, pp. 9-21.
3. Grossman CJ, Wiseman J, Lucas FS, *et al*: Inhibition of constitutive and inducible cyclooxygenase activity in human platelets and mononuclear cells by NSAIDs and COX-2 inhibitors. *Inflammation Research* 44:253-257, 1995.
4. Ricketts AP, Lundy KM, Siebel SB: Evaluation of selective inhibition of canine cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs. *Am J Vet Res* 59:11, pp. 1441-1446, November 1998.

5. Ceuppens JL, *et al*: Non-steroidal anti-inflammatory agents inhibit the synthesis of IgM rheumatoid factor *in vitro*. *Lancet* 1:528, 1982.
6. Ceuppens JL, *et al*: Endogenous prostaglandin E<sub>2</sub> enhances polyclonal immunoglobulin production by ionically inhibiting T suppressor cell activity. *Cell Immunol* 70:41, 1982.
7. Schleimer RP, *et al*: The effects of prostaglandin synthesis inhibition on the immune response. *Immunopharmacology* 3:205, 1981.
8. Leung KH, *et al*: Modulation of the development of cell mediated immunity: possible roles of the products of cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism. *Int J Immunopharmacology* 4:195, 1982.
9. Veit BC: Immunoregulatory activity of cultured-induced suppressor macrophages. *Cell Immunol* 72:14, 1982.
10. Schmitt M, *et al*: Biopharmaceutical evaluation of carprofen following single intravenous, oral, and rectal doses in dogs. *Biopharm Drug Dispos* 11(7): 585-94, 1990.
11. Kore AM: Toxicology of nonsteroidal anti-inflammatory drugs. *Veterinary Clinics of North America, Small Animal Practice* 20, March 1990.
12. Binns SH: Pathogenesis and pathophysiology of ischemic injury in cases of acute renal failure. *Compend for Cont Ed* 16:1, January 1994.
13. Boothe DM: Prostaglandins: Physiology and clinical implications. *Compend for Cont Ed* 6:11, November 1984.
14. Rubin SI: Nonsteroidal anti-inflammatory drugs, prostaglandins, and the kidney. *JAVMA* 188:9, May 1986.
15. Ko CH, Lange DN, Mandsager RE, *et al*: Effects of butorphanol and carprofen on the minimal alveolar concentration of isoflurane in dogs. *JAVMA* 217:1025-1028, 2000.

For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Intervet Inc. at 1-800-441-8272.

ANADA # (To be determined), Approved by FDA



EXPECT MORE™

Manufactured for:

INTERVET INC.

Millsboro, DE 19966

Made in Austria

**Dog Owner Information about “Trade Name” Chewable Tablets (carprofen)**  
“Trade Name” (pronounced “TBD”) for Osteoarthritis and Post-Surgical Pain  
Generic name: carprofen (“car-prō-fen”)

This summary contains important information about “Trade Name”. You should read this information before you start giving your dog “Trade Name” 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 “Trade Name”.

**What is “Trade Name”?**

“Trade Name” 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. “Trade Name” is a prescription drug for dogs. It is available as a 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 “Trade Name” 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 “Trade Name”?**

While “Trade Name” 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 “Trade Name” is discontinued or not given as directed, your dog's pain and inflammation may come back.

**Who should not take “Trade Name”?**

Your dog should not be given “Trade Name” if he/she:

- Has had an allergic reaction to carprofen, the active ingredient of “Trade Name”.

- 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.

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

#### **How to give “Trade Name” to your dog.**

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

#### **What to tell/ask your veterinarian before giving “Trade Name”.**

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 “Trade Name” is prescribed.
- How often your dog may need to be examined by your veterinarian.
- The risks and benefits of using “Trade Name”.

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

- Experienced side effects from “Trade Name” 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 “Trade Name” therapy?**

“Trade Name”, like other drugs, may cause some side effects. Serious but rare side effects have been reported in dogs taking NSAIDs, including “Trade Name”. 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 "Trade Name" 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 "Trade Name" therapy. If you have additional questions about possible side effects, talk to your veterinarian.

#### **Can "Trade Name" be given with other medicines?**

"Trade Name" 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 "Trade Name". 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 "Trade Name"?**

Contact your veterinarian immediately if your dog eats more than the prescribed amount of "Trade Name".

#### **What else should I know about "Trade Name"?**

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

As with all prescribed medicines, "Trade Name" 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 "Trade Name" at

regular checkups. Your veterinarian will best determine if your dog is responding as expected and if your dog should continue receiving "Trade Name".

To report a suspected adverse reaction, call Intervet Inc. at 1-800-441-8272.

Issued "Month 200X"



Manufactured for:

INTERVET INC.

Millsboro, DE 19966

Made in Austria

Pioneer Labeling

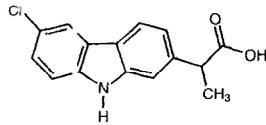
# RIMADYL

## Carprofen

### Tablets

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

**CAUTION:** For oral use only. This drug is for use by or on the order of a licensed veterinarian.  
**DESCRIPTION:** Rimadyl (carprofen) is a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class. The active ingredients are carprofen, the nonproprietary designation, and its racemic enantiomers, (S)-(+)-carprofen and (R)-(-)-carprofen. The chemical structure of carprofen is shown below.



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-nerve, non-steroidal anti-inflammatory agent with characteristic analgesic and antipyretic activity approximately equivalent to indomethacin in animal models.

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. The one coded for by cyclooxygenase-1 (COX-1) synthesizes prostaglandins necessary for normal gastrointestinal 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. In an *in vitro* study using canine cell culture, carprofen demonstrated selective inhibition of COX-2 versus COX-1. Clinical relevance of these data has not been shown. Carprofen has also been shown to inhibit the release of several pro-inflammatory mediators in two inflammatory cell systems: rat polymorphonuclear leukocytes (PMN) and human neutrophil-derived cells, indicating inhibition of acute (PMN system) and chronic (neutrophil system) inflammatory actions.

Several studies have demonstrated that carprofen has modulatory effects on both humoral and cellular immune responses. Data also indicate that carprofen inhibits the production of osteoclast-activating factor (OAF), PGE<sub>2</sub>, and PGE<sub>2</sub> by its inhibitory effects on prostaglandin biosynthesis.

Based upon comparison with data obtained from intravenous administration, carprofen is rapidly and nearly completely absorbed (more than 90% bioavailable) when administered orally. 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 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. Rimadyl is more than 93% bound to plasma protein and exhibits a very small volume of distribution.

Carprofen is eliminated in the dog primarily by both transformation in the liver followed by rapid excretion in the excretory metabolites, 7-hydroxy carprofen and the other glucuronides and 2 phenolic metabolites, 7-hydroxy carprofen and 8-hydroxy carprofen in the feces (70-90%) and urine (10-20%). Some orthohepatic circulation of the drug is observed.

**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.

**DOSEAGE 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 dosage 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.

**EFFECTIVENESS:** Confirmation of the effectiveness of Rimadyl for the relief of pain and inflammation associated with osteoarthritis, and for the control of postoperative pain associated with soft tissue and orthopedic surgeries was demonstrated in 5 placebo-controlled, masked studies examining the anti-inflammatory and analgesic effectiveness of Rimadyl caplets in various breeds of dogs.

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

Separate placebo-controlled, masked, multicenter field studies confirmed the effectiveness of Rimadyl caplets for the control of postoperative pain when dosed at 2 mg/lb once daily in various breeds of dogs. In these studies, dogs undergoing orthopedic surgery, cruciate ligament and arthralgias were administered Rimadyl preoperatively and for a maximum of 3 days (soft tissue) or 4 days (orthopedic) postoperatively. In general, dogs administered Rimadyl showed statistically significant improvement in pain scores compared to controls.

**ANIMAL SAFETY - STUDIES:** Laboratory studies in unanesthetized dogs and clinical field studies have demonstrated that Rimadyl is well tolerated in dogs after oral administration.

In target animal safety studies, Rimadyl 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 12 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 8-week treatment period, black or bloody stools were observed in 1 dog (1 incident) treated with 1 mg/lb twice daily and 1 dog (1 incident) 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 hypalbuminemia. 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 pathological examination. Histologic examination 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 12 and 52 weeks, respectively, dogs were administered orally up to 11.4 mg/lb/day (5 times the recommended total daily dose of 2 mg/lb) of carprofen. In both studies, there was well-tolerated toxicity 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 amino transferase (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 548 dogs of different breeds at the recommended oral doses for 14 days (391 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 Rimadyl-treated animals was no higher than placebo-treated animals (placebo contained inactive ingredients found in Rimadyl). Female 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 Rimadyl and placebo, respectively. Difference 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 Rimadyl and placebo, respectively. In the latter study, 3 Rimadyl-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.

Clinical field studies were conducted in 291 dogs of different breeds undergoing orthopedic or soft tissue surgery. Dogs were administered 2 mg/lb of Rimadyl two hours prior to surgery then once daily, as needed for 2 days (soft tissue surgery) or 3 days (orthopedic surgery). Rimadyl was well tolerated when used in conjunction with a variety of anesthetic-related drugs. The type and severity of abnormal health observations in Rimadyl- 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 Rimadyl- and placebo-treated animals. Changes in clinicopathologic indices of hematopoiesis, 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 Rimadyl and placebo, respectively. The mean post-treatment AST values were 3.1 IU less for dogs receiving Rimadyl and 0.2 IU greater for dogs receiving placebo.

**CONTRAINDICATIONS:** Rimadyl 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. 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 adverse effects in patients with underlying or pre-existing disease more often than in healthy patients. 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. The use of parenteral fluids during surgery should be considered to reduce the potential risk of renal complications when using NSAIDs preoperatively.

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. Concomitant administration of potentially nephrotoxic drugs should be approached cautiously, with appropriate monitoring. Since many

very closely monitored. Sensitivity to drug-associated adverse reactions varies among individual patients. For example, Rimadyl treatment was not associated with renal toxicity or gastrointestinal ulceration in well-controlled safety studies of up to ten times the dose in dogs.

Rimadyl 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 Rimadyl in animals less than 6 weeks of age, pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. Studies to determine the safety of Rimadyl 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. Additional pain medication is warranted after administration of the total daily dose of Rimadyl. Intravenous analgesia should be considered. The use of another NSAID is not recommended.

#### FORMATION FOR DOG OWNERS

Rimadyl, 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 Rimadyl 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 of osteoarthritis with 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- 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 of osteoarthritis with once daily administration of 2 mg/lb. The following categories of abnormal health observations were reported. The product vehicle served as control.

Observation*	Rimadyl (n=129)	Placebo (n=132)
Inappetence	1.6	0
Vomiting	3.1	5.8
Diarrhea/Soft stool	1.1	4.5
Behavior change	0.8	0.8
Dermatitis	0.8	0.8
PUPPD	0.8	0
SAP increase	7.8	8.3
ALT increase	4.5	4.5
AST increase	2.3	0.8
BUN increase	1.1	1.5
Ribulurium	16.3	12.1
Ketamine	14.7	9.1

Clinical pathology parameters listed represent reports of increases from pre-treatment values; medical judgement is necessary to determine clinical relevance. During investigational studies of surgical pain for the caplet formulation, no clinically significant adverse reactions were reported. The product vehicle served as control.

#### Percentage of Dogs with Abnormal Health Observations Reported in Surgical Pain Field Studies with Caplets (2 mg/lb/once daily)

Observation*	Rimadyl (n=148)	Placebo (n=149)
Vomiting	10.1	13.6
Diarrhea/soft stool	5.1	6.0
Ocular disease	2.7	0
Inappetence	1.4	0
Dermatitis/skin lesion	2.0	1.3
Dysrhythmia	2.7	4.0
Apnea	1.4	0
Oral/peridontal disease	1.4	0
Pyrexia	0.7	1.3
Urinary tract disease	1.4	1.3
Wound drainage	1.4	0

\* A single dog may have experienced more than one occurrence of an event.

† 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 tests, hyperbilirubinemia, bilirubinuria, hypobuntenemia. 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, proteinuria.

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

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

**Dermatologic:** Pruritus, increased shedding, alopecia, pyodermatitis (most dermatitis hot spots), necrotizing panniculitis/vesiculitis, 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 1-800-366-5288.

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

**HOW SUPPLIED:** Rimadyl caplets are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per caplet. Each caplet size is packaged in bottles containing 14, 60, or 180 caplets.

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For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Pfizer Animal Health at 1-800-366-5288.

NADA #141-053, Approved by FDA

Distributed by  

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

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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.

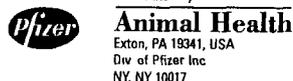
As with all prescribed medicines, Rimadyl should only be given to the dog for which it was prescribed. It should be given to your dog only for the condition for which it was prescribed.

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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Keep out of reach of children. Not for human use. 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).

Pfizer Health Care, Inc.  
New York, NY 10017



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