

NOV 7 2007

Approval Date: _____

FREEDOM OF INFORMATION SUMMARY

**ORIGINAL ABBREVIATED NEW ANIMAL DRUG
APPLICATION**

ANADA 200-397

VETPROFEN

(carprofen)

Caplets

**Indicated for the relief of pain and inflammation associated with
osteoarthritis and the control of postoperative pain associated
with soft tissue and orthopedic surgeries in dogs**

**Sponsored by:
Belcher Pharmaceuticals, Inc.**

2007-200-397

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FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-397
- b. Sponsor: Belcher Pharmaceuticals, Inc.
12393 Belcher Road, Suite 420
Largo, FL 33773
- Drug Labeler Code: 062250
- c. Established Name: Carprofen
- d. Proprietary Name: VETPROFEN
- e. Dosage Form: Caplets
- f. How Supplied: 25 mg bottles of 30, 60 and 240 caplets
75 mg bottles of 30, 60 and 240 caplets
100 mg bottles of 30, 60 and 240 caplets
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: 25 mg, 75 mg, and 100 mg
- i. Route of Administration: Oral
- j. Species/Class: Dogs
- k. Recommended Dosage: 2 mg/lb (4.4 mg/kg) of body weight. 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.
- l. Pharmacological Category: Non-steroidal anti-inflammatory drug (NSAID)
- m. Indications: VETPROFEN 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.
- 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

Objective: The objective of this study was to determine the comparative *in vivo* blood-level bioequivalence of Belcher Pharmaceuticals, Inc.'s 25 mg VETPROFEN (carprofen) caplets and Pfizer, Inc.'s 25 mg RIMADYL Caplets in dogs.

Investigator: Midwest Research Institute (MRI)
425 Volker Boulevard
Kansas City, Missouri

Study Design: The design was a 2-treatment, 2-period crossover. The treatment sequences (groups) were: A = RIMADYL followed by VETPROFEN and B = VETPROFEN followed by RIMADYL.

Summary: Twelve beagle dogs (6 males (M) and 6 females (F)) were randomly assigned to two treatment groups containing 6 animals (3M + 3F). The animals were fasted 16 ± 4 hours prior to dose administration and approximately 4 hours post-dose. Treatments were administered orally on day 1 in period 1 and day 18 in period 2 at a dose rate of 4.4 mg carprofen/kg body weight. Dogs were weighed within 1 day prior to treatment. A washout period from day 8 to day 17 was observed. Approximately 5 mL of blood was collected at approximately 0 (pre-dose), 0.25, 0.5, 1, 2, 3, 4, 6, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours. In total, 17 blood samples were taken from each dog in each treatment period. All blood samples collected were processed for carprofen analysis using a fully validated analytical method.

Results: The area under the curve was estimated using the trapezoidal rule including data from time 0 to the last sampling time associated with quantifiable drug concentrations (AUC). The maximum concentration measured for all time periods (C_{MAX}) was estimated. The natural logarithm of both AUC and C_{MAX} was computed and used as the variable for analysis.

The criteria for determining bioequivalence, 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 AUC and C_{MAX} and then take the anti-log of the confidence limits multiplied by 100. The resulting bounds should be between 80.00% and 125.00%. As seen in the table below, both AUC and C_{MAX} fall within those bounds.

Variable	Belcher Mean	Pfizer Mean	Lower Bound	Upper Bound
AUC (µg*hr/mL)	297.8*	297.2*	85.22%	117.82%
C _{MAX} (µg/mL)	34.3*	33.6*	88.03%	118.01%
T _{MAX} (hr)	2.00 [†]	1.88 [†]	NA	NA

* Geometric Mean

[†] Arithmetic Mean

Conclusions: The variable time to maximum concentration (T_{MAX}) is permitted to be interpreted by clinical judgment. In this case, there is no reason to expect the difference in T_{MAX} will affect the efficacy of the drug since both AUC and C_{MAX} are bioequivalent and the product is administered as a single dose.

Because both AUC and C_{MAX} are bioequivalent and T_{MAX} is acceptable, the study objective to determine the bioequivalence of the generic and pioneer products was achieved.

B. Dissolution Study

Objective: *In vitro* dissolution data were submitted in support of a request for waiver of *in vivo* bioequivalence study requirements for the 75 mg and 100 mg strength caplets. The 25 mg strength tablets were the subject of the *in vivo* bioequivalence trial.

Investigator: Belcher Pharmaceutical, Inc.
6911 Bryan Dairy Road
Largo, FL

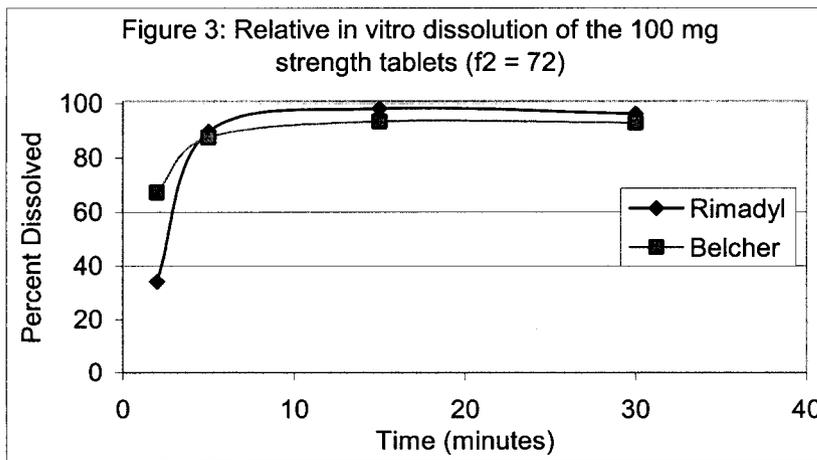
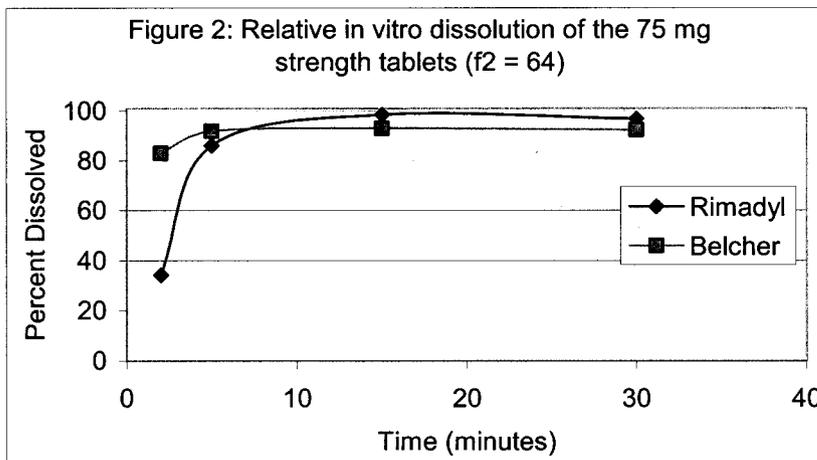
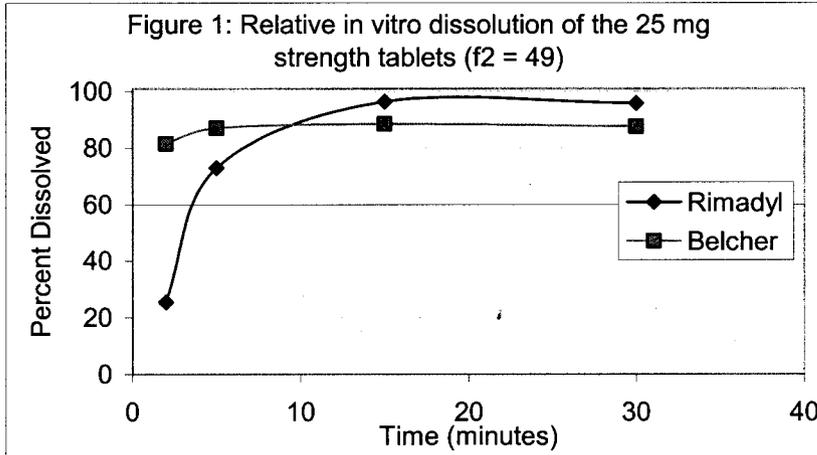
Study Design: Twelve tablets of each product strength were examined using USP dissolution apparatus 2 (paddle) at 50 rpm. The dissolution medium was simulated intestinal fluids without enzyme, pH 7.5. This is the same method that has been used for quality control purposes for RIMADYL caplets. Samples were taken at 2, 5, 15 and 30 minutes of testing and the carprofen concentrations were determined by HPLC. The percent drug released from each strength and for each formulation was calculated at each time point.

Similarity of profiles was based upon the model-free approach defined in CDER's 8/97 guidance for industry titled "Dissolution Testing of Immediate Release Dosage Forms". In brief, the similarity factor (f₂) used for confirming comparability is defined 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 f₂ values are equal to or greater than 50.

Results: The value for f_2 and the relative dissolution profiles for the test and reference products are provided in Figures 1 – 3.



Although slight test-reference differences were seen across tablet strengths at the 2 minute sample, differences in dissolution at these very early time points are rarely considered to have any clinical significance. Therefore, only the time points of 5 – 30 minutes have been included in our evaluation.

Conclusions: A slightly slower *in vitro* dissolution rate for the Belcher 25 mg strength caplets as compared to the 25 mg RIMADYL caplets is inconsequential because the two products have been shown to be bioequivalent based upon *in vivo* test results. Based upon the *in vitro* dissolution test results, CVM concludes that the Belcher 75 mg and 100 mg strength carprofen caplets are eligible for a waiver of *in vivo* bioequivalence study requirements.

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.

Human Warnings are provided on the product label as follows:

Keep out of the reach of children.

Not for human use.

Consult a physician in cases of accidental ingestion by humans.

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that the product VETPROFEN, 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 indicated below:

Generic Labeling for ANADA 200-397:

VETPROFEN –

 Dog Owner Information Sheet

 Package Insert

 25 mg bottles of 30, 60 and 240 caplets

 75 mg bottles of 30, 60 and 240 caplets

 100 mg bottles of 30, 60 and 240 caplets

Pioneer Labeling for NADA 141-053:

RIMADYL –

Dog Owner Information Sheet

Package Insert

25 mg bottles of 30, 60 and 180 caplets

75 mg bottles of 30, 60 and 180 caplets

100 mg bottles of 30, 60 and 180 caplets

Vetprofen™ (carprofen) Caplets

**DOG OWNER
INFORMATION**
-DO NOT REMOVE-



Dog Owner Information about Vetprofen™ Caplets (carprofen)

Vetprofen™ (pronounced "Vet-prō-fen")
for Osteoarthritis and Post-Surgical Pain
Generic name: carprofen ("car-prō-fen")

This summary contains important information about Vetprofen. You should read this information before you start giving your dog Vetprofen 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 Vetprofen.

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

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

What is Vetprofen?

Vetprofen 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. Vetprofen is a prescription drug for dogs. 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

To control surgical pain (e.g. for surgeries such as spays, ear procedures or orthopedic repairs) your veterinarian may administer Vetprofen 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 Vetprofen?

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

Who should not take Vetprofen?

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

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

Vetprofen should be given to dogs only.

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

How to give Vetprofen to your dog.

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

What to tell/ask your veterinarian before giving Vetprofen.

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

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

- Experienced side effects from Vetprofen 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.

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 Vetprofen 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 Vetprofen therapy. If you have additional questions about possible side effects, talk to your veterinarian.

Can Vetprofen be given with other medicines?

Vetprofen should not be given with other NSAIDs (for example, aspirin, deracoxib, etodolac, firocoxib, meloxicam, tepoxalin) or steroids (for example, cortisone, dexamethasone, prednisone, 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 Vetprofen. 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 Vetprofen?

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

What else should I know about Vetprofen?

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

As with all prescribed medicines, Vetprofen 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 Vetprofen at regular check ups. Your veterinarian will best determine if your dog is responding as expected and if your dog should continue receiving Vetprofen.

To report a suspected adverse reaction call 1-800-835-9496

Issued July 2007

Manufactured by:

Belcher Pharmaceuticals, Inc.

12393 Belcher Road, Suite 420

Largo, Florida 33773

Distributed by:

Vétoquinol U.S.A., Inc.

Buena, NJ 08310

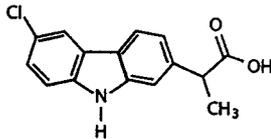
Vetprofen™ (carprofen) Caplets

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.

DESCRIPTION: Vetprofen (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- α -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.¹

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.² 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.³ In an *in vitro* study using canine cell cultures, carprofen demonstrated selective inhibition of COX-2 versus COX-1.⁴ 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.¹

Several studies have demonstrated that carprofen has modulatory effects on both humoral and cellular immune responses.^{5,6} Data also indicate that carprofen inhibits the production of osteoclast-activating factor (OAF), PGE₁, and PGE₂ by its inhibitory effects on prostaglandin biosynthesis.¹

Based upon comparison with data obtained from intravenous administration, carprofen is rapidly and nearly completely absorbed (more than 90% bioavailable) when administered orally.¹⁰ 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: Vetprofen 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.

CONTRAINDICATIONS: Vetprofen should not be used in dogs exhibiting previous hypersensitivity to carprofen.

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, Adverse Reactions, Animal Safety and Post-Approval Experience).

PRECAUTIONS: As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic 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.¹¹⁻¹⁴ 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.¹²⁻¹⁴ 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.¹¹⁻¹⁴ 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 inhaled anesthetics needed.¹⁶

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. Consider appropriate washout times when switching from one NSAID to another or when switching from corticosteroid use to NSAID use.

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 1-800-835-9496.

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. Caplets are scored and dosage should be calculated in half-caplet 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 caplets in various breeds of dogs.

Separate placebo-controlled, masked, multicenter field studies confirmed the anti-inflammatory and analgesic effectiveness of carprofen 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 carprofen at labeled doses.

Separate placebo-controlled, masked, multicenter field studies confirmed the effectiveness of carprofen caplets 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 compared to controls.

ANIMAL SAFETY: 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 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 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.

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

HOW SUPPLIED: Vetprofen caplets are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per caplet. Each caplet size is packaged in bottles containing 30, 60, or 240 caplets.

Some enterohepatic circulation of the drug is observed.

INDICATIONS: Vetprofen 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.

CONTRAINDICATIONS: Vetprofen should not be used in dogs exhibiting previous hypersensitivity to carprofen.

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, Adverse Reactions, Animal Safety and Post-Approval Experience).

PRECAUTIONS: As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic 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.¹¹⁻¹⁴ 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.^{12,14} 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.¹¹⁻¹⁴ 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.¹⁵

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. Consider appropriate washout times when switching from one NSAID to another or when switching from corticosteroid use to NSAID use.

INFORMATION FOR DOG OWNERS:

Vetprofen, 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 Vetprofen 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.

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)

Observation	Carprofen (n=120)	Placebo (n=132)
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 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*	Carprofen (n=148)	Placebo (n=149)
Vomiting	10.1	13.4
Diarrhea/Soft stool	6.1	6.0
Ocular disease	2.7	0
Inappetence	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

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 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.

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

HOW SUPPLIED: Vetprofen caplets are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per caplet. Each caplet size is packaged in bottles containing 30, 60, or 240 caplets.

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For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call: 1-800-835-9496. ANADA # 200-397, Approved by FDA.



Manufactured by:
Belcher Pharmaceuticals, Inc.
12393 Belcher Road, Suite 420
Largo, Florida 33773

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

July 2007
Printed in USA

L071-VET

R-0707

Each scored caplet contains 25 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Bayer Pharmaceuticals, Inc.
Largo, Florida 33773



Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Bueno, NJ 08310

1309L-01-VET R-0706

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

NDC 62250-309-01

Vetprofen™

(carprofen) 25 mg

Non-Steroidal
Anti-inflammatory Drug

For Oral Use
in Dogs Only



30 caplets

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).

TAKE TIME



OBSERVE LABEL DIRECTIONS



0 62250 30901 2

Batch #
Exp. Date



PANTONE 292 C



PANTONE 354 C



PANTONE 485 C



BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 25 mg of carprofen.

INDICATIONS:
Vetprofen™ 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:
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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Bayer Pharmaceutical, Inc.
Largo, Florida 33773
Bayer
Made in USA

Distributed by:
Vetoquinol U.S.A., Inc.
Burlington, NJ 08310
L309L-13-VET 8-0706

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

NDC 62250-309-13

 **Vetoquinol**

ANADA # 200-397
Approved by FDA

Vetprofen™

(carprofen) 25 mg

Non-Steroidal
Anti-Inflammatory Drug

For Oral Use
in Dogs Only



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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date

 PANTONE 292 C

 PANTONE 354 C

 PANTONE 485 C

 BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 25 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Betcher Pharmaceuticals, Inc.
Largo, Florida 33773

 Betcher

Made in USA

Distributed by:
Vetoquinol U.S.A., Inc.
Buena, NJ 08310

 Vetoquinol

L309L14-VET R-0706

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

NDC 62250-309-14

 Vetoquinol

ANADA # 200-397
Approved by FDA

Vetprofen™

(carprofen) 25 mg

Non-Steroidal
Anti-Inflammatory Drug

For Oral Use
in Dogs Only



WARNINGS:

Keep out of reach of children. Not for human use. Consult a physician in case 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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date

 PANTONE 292 C

 PANTONE 354 C

 PANTONE 485 C

 BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 75 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Belcher Pharmaceuticals, Inc.
Largo, Florida 33773

Belcher
Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

L310L-01-VET R-0706

Vetprofen™

(carprofen) 75 mg

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.

Vétoquinol

ANADA # 200-397
Approved by FDA

NDC 62250-310-01

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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date



PANTONE 3275 C



PANTONE 354 C



PANTONE 485 C



BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 75 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
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Largo, Florida 33773


Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

L310L-13-VET R-0706

Non-Steroidal
Anti-Inflammatory Drug

For Oral Use
in Dogs Only

Vetprofen™
(carprofen) 75 mg



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

NDC 62250-310-13

 Vétoquinol

ANADA # 200-397
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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date

 PANTONE 3275 C

 PANTONE 354 C

 PANTONE 485 C

 BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 75 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Belcher Pharmaceuticals, Inc.
Largo, Florida 33773

Belcher
Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

L310L-14-VET R-0706

Vetprofen™

(carprofen) 75 mg

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.

Vétoquinol

ANADA # 200-397
Approved by FDA

NDC 62250-310-14

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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date

PANTONE 3275 C

PANTONE 354 C

PANTONE 485 C

BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 100 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Belcher Pharmaceuticals, Inc.
Largo, Florida 33773

Belcher
Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

L311L-01-VET R-0706

Vetprofen™

(carprofen) 100 mg

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.

 Vétoquinol

ANADA # 200-397
Approved by FDA

NDC 62250-311-01

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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date

 PANTONE 266 C

 PANTONE 354 C

 PANTONE 485 C

 BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 100 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Belcher Pharmaceuticals, Inc.
Largo, Florida 33773

Belcher
Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

L311L-13-VET R-0706

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.

NDC 62250-311-13

 Vétoquinol

ANADA # 200-397
Approved by FDA

Vetprofen™

(carprofen) 100 mg

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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #
Exp. Date

 PANTONE 266 C

 PANTONE 354 C

 PANTONE 485 C

 BLACK

NON VARNISH AREA - DO NOT PRINT

Each scored caplet contains 100 mg of carprofen.

INDICATIONS:

Vetprofen™ 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:

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. Caplets are scored and dosage should be calculated in half-caplet increments.

Manufactured by:
Belcher Pharmaceuticals, Inc.
Largo, Florida 33773

Belcher
Made in USA

Distributed by:
Vétoquinol U.S.A., Inc.
Buena, NJ 08310

L311L-14-VET R-0706

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.

NDC 62250-311-14

 Vétoquinol

ANADA # 200-397
Approved by FDA

Vetprofen™

(carprofen) 100 mg

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).

TAKE TIME



OBSERVE LABEL
DIRECTIONS



Batch #

Exp. Date

 PANTONE 266 C

 PANTONE 354 C

 PANTONE 485 C

 BLACK

NON VARNISH AREA - DO NOT PRINT

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 deracoxib, etodolac, firocoxib, meloxicam, phenylbutazone or tepoxalin) 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, deracoxib, etodolac, firocoxib, meloxicam, tepoxalin) or steroids (for example, cortisone, dexamethasone, prednisone, 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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RIMADYL[®]

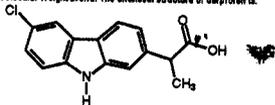
(carprofen)
Capslets

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: Rimadyl (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 carboxylic acid, 6-chloro-*n*-methyl-*m*-carboxanilic-acidic acid. The empirical formula is C₁₇H₁₅ClNO₂ and the molecular weight is 272.72. 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 equiptotent 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 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 drug to drug. In an *in vitro* study using canine cell cultures, carprofen demonstrated selective inhibition of COX-2 versus COX-1. Clinical relevance of this data has not been shown. Carprofen has also been shown to inhibit the release of several proinflammatory cytokines from polymorphonuclear leukocytes (PMN) and human mononuclear synovial cells, indicating inhibition of acute (PMN) and chronic (synovial cell system) inflammatory reactions.

Several studies have demonstrated that carprofen has modulatory effects on both humoral and cellular immune responses.^{1,2} Data also indicates that carprofen inhibits the production of osteoclast-activating factor (OAF), PGE₂, and PGE₁ by its inhibitory effects on prostaglandin biosynthesis.³

Based upon comparison with data obtained from intravenous administration, carprofen is rapidly and nearly completely absorbed (mean drug bioavailability) when administered as oral capsules. Blood plasma concentrations are achieved in ~1.3 hours after oral administration of 1, 2, and 25 mg/kg to dogs. The mean terminal half-life of carprofen is approximately 8 hours (range 4.5-9.5 hours) after single oral doses ranging from 1-25 mg/kg of body weight. After a 10 mg/kg single dose, the mean elimination half-life was approximately 11.7 hours in the dog. Rimadyl is more than 90% 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 in the urine. The major metabolites of carprofen and the other proenolones of 2-phenoxyacetamide, 7-hydroxy carprofen and 4-hydroxy carprofen in the feces (70-80%) and urine (10-20%) form an important route of elimination of the drug in dogs.

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.

CONTRAINDICATIONS: Rimadyl should not be used in dogs exhibiting previous hypersensitivity to carprofen.

WARNINGS: Keep out of reach of children. Not for human use. Consult a physician in case 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 baseline data 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, Adverse Reactions, Animal Safety and Precautions).

PRECAUTIONS: As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Effects may result from decreased prostaglandin production and inhibition of the enzyme cyclooxygenase which is essential for the formation of prostaglandins from arachidonic acid.¹⁻¹⁴ When NSAIDs inhibit prostaglandins that cause inflammation they may also inhibit those prostaglandins which maintain normal homeostatic function. Those anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing diseases more often than in healthy patients.^{1,2,4} NSAID therapy could mask early signs of disease which has previously been undiagnosed due to the absence of apparent clinical signs. Patients with underlying renal disease for example, may experience azotemia or decomposition of their renal disease while on NSAID therapy.¹⁻¹⁴ 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 this class, adverse reactions may occur with its use. The most frequently reported effects have been gastrointestinal signs. Events involving upper and lower gastrointestinal, 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 chronic, congestive heart failure. Concomitant 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 Rimadyl with other anti-inflammatory drugs, such as corticosteroids and NSAIDs, should be avoided or very closely monitored. Caution to drug-associated adverse reactions varies with the individual patient. 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 16 weeks of age, appropriate for breeding purposes, or in breeding females has not been established. Studies to determine the safety of Rimadyl during pregnancy and lactation with other protein-bound and similarly metabolized drugs have not been conducted. Drug compatibility should be monitored closely in patients receiving additional therapy. Such drugs potentially used include cardiac, anticonvulsant and behavioral medications. It has been suggested that treatment with carprofen may reduce the level of analgesic anesthesia needed.¹⁵

If additional pain medication is warranted after administration of the total daily dose of Rimadyl, alternative analgesia should be considered. The use of another NSAID is not recommended. Caution is appropriate without times when switching from one NSAID to another or when switching from corticosteroid use to NSAID use.

INFORMATION 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 whites of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. Serious adverse reactions associated with this drug occur more often 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 recover 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.

ADVERSE REACTIONS: During investigational studies of osteoarthritis with twice daily administration of 1 mg/kg, no clinically significant adverse reactions were reported. Some clinical signs were observed during field studies (n=257) 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 (2%), lethargy (1%), behavioral changes (1%), and excretion (0.2%). The product vehicle served as control. There were no serious adverse events reported during blinded field studies of osteoarthritis with once daily administration of 2 mg/kg. 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/kg once daily)		
Observation	Rimadyl (n=128)	Placebo (n=122)
Inappetence	1.1	1.6
Vomiting	3.1	2.5
Diarrhea/Soft stool	3.1	4.5
Behavior change	0.8	0.8
Dermatitis	0.8	0.8
PUPD	0.8	0.8
SAP increase	0.8	0.8
ALT increase	5.4	4.9
AST increase	2.3	2.3
BUN increase	3.1	3.3
Strabismus	10.2	12.1
Xenotoma	14.7	8.1

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 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/kg once daily)		
Observation	Rimadyl (n=16)	Placebo (n=16)
Vomiting	10.1	11.3
Diarrhea/Soft stool	2.7	6.0
Ocular disease	1.4	0
Inappetence	2.0	0
Dermatitis/skin lesion	0.7	0
Dysrhythmia	0.7	0
Agonia	1.4	0
Oral/peridontal disease	1.4	0
Pyrexia	0.7	1.3
Urinary tract disease	1.4	0
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, melena, hematemesis, gastrointestinal ulceration, gastrointestinal bleeding, gastroenteritis.

Hepatic: Inappetence, vomiting, jaundice, acute hepatic failure, hepatic enzyme elevation, abnormal liver function tests, hyperbilirubinemia, bilirubinuria, hypocoagulability. 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, hyperexcitability, restlessness, aggressiveness.

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

Dermatologic: Pruritus, increased shedding, alopecia, pyoderma, moist dermatitis (hot spots), non-healing panniculitis/vacuolitis, ventral eczematosis.

Immunologic or hypersensitivity: Facial swelling, hives, erythema.

In rare instances, death has been associated with some of the adverse reactions listed above. To report a suspected adverse reaction, please call 1-800-368-8289.

DOSEAGE AND ADMINISTRATION: Always provide clear information sheet with prescription. The recommended dosage for oral administration to dogs is 2 mg/kg (4.4 mg/kg) of body weight daily. The total daily dose may be administered as 2 mg/kg of body weight once daily or divided and administered as 1 mg/kg (2.2 mg/kg) twice daily. For the control of postoperative pain, administer approximately 2 hours before the procedure. Capslets are scored and dosage should be calculated in half-capslet increments.

EFFECTS: 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 6 placebo-controlled, masked studies examining the anti-inflammatory and analgesic effectiveness of Rimadyl capsules in various breeds of dogs.

Separate placebo-controlled, masked, multicenter field studies confirmed the anti-inflammatory and analgesic effectiveness of Rimadyl capsules when dosed at 2 mg/kg once daily or when divided and administered at 1 mg/kg twice daily. In these field studies, dogs diagnosed with osteoarthritis showed statistically significant 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 capsules for the control of postoperative pain when dosed at 2 mg/kg once daily in various breeds of dogs. In these studies, dogs were dosed with Rimadyl capsules prior to and after surgery. Dogs 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 placebo-treated dogs.

ANIMAL SAFETY: 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 in healthy Beagle dogs at 1, 3, and 10 mg/kg twice daily for 1, 2, and 4 weeks. The recommended dose of 2 mg/kg twice daily was associated with no significant adverse reactions. Serum albumin for a single female dog receiving 1 mg/kg twice daily decreased to 2.1 g/dl after 2 weeks of treatment, returned to the pre-treatment value (2.6 g/dl) after a week of treatment, and was 2.4 g/dl at the 4-week treatment. Over the 4-week treatment period, blood or bloody stools were observed in 1 dog (1 incidence) treated with 1 mg/kg twice daily and 1 male that received 3 mg/kg twice daily. Reduction of the colonic mucosa was observed in 1 male that received 3 mg/kg twice daily.

Two of 8 dogs receiving 10 mg/kg orally twice daily (10 times the recommended total daily dose) for 14 days exhibited hyperalbuminemia. The mean albumin level in the dogs receiving this dose was lower (2.36 g/dl) than each of the placebo-treated groups (2.8 and 3.0 g/dl, respectively). Two incidences of black or bloody stool were observed in 1 dog. Five of 8 dogs exhibited reddened areas of duodenal mucosa on endoscopic examination. Histologic examination of these areas revealed no evidence of ulceration, but did show minimal congestion of the lamina propria in 2 of the dogs.

In separate safety studies lasting 13 and 82 weeks, respectively, dogs were administered orally up to 11.4 mg/kg/day (5.7 times the recommended total daily dose of 2 mg/kg) of carprofen. In both studies, the drug was well tolerated, with no deaths reported. The highest dose was associated with an increase in serum L-aspartate aminotransferase (ALT) of approximately 20 IU.

In the 82-week study, minor dermatologic changes occurred in dogs in each of the treatment groups but not in the control group. 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 84 dogs of different breeds at the recommended oral doses for 14 days (27 dogs were included in a study evaluating 1 mg/kg twice daily and 252 dogs were included in a separate study evaluating 2 mg/kg once daily). In both studies the drug was clinically well tolerated. The incidence of clinical adverse reactions in Rimadyl-treated animals was no higher than placebo-treated animals (placebo-treated animals received 1 mg/kg greater and 8 IU less than the recommended value for dogs receiving Rimadyl) and placebo, respectively. Differences were not statistically significant. For animals receiving 2 mg/kg once daily, the mean post-treatment serum ALT values were 43 IU greater and 23 IU less than pre-treatment values for dogs receiving Rimadyl and placebo, respectively. For 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 3-fold increase in ALT. None of these animals showed clinical signs associated with laboratory test abnormalities. Clinicians in the clinical laboratory values (therapeutic and clinical chemistry) were not considered clinically significant. The 1 mg/kg twice daily course of therapy was repeated as needed at 10 mg/kg intervals in 244 dogs, some for as long as 8 years.

Clinical field studies were conducted in 897 dogs of different breeds undergoing orthopedic or soft tissue surgery. Dogs were administered 2 mg/kg of Rimadyl two hours prior to surgery (twice daily, as needed) for 2 days (soft tissue surgery) or 3 days (orthopedic surgery). Rimadyl was well tolerated and had no effect on analgesia with a variety of analgesic-related drugs. The type and severity of abnormal health observations in Rimadyl- and placebo-treated animals were approximately equal and low in number (see Adverse Reactions). The most frequent abnormal health observation was vomiting and was observed with approximately the same frequency in Rimadyl- and placebo-treated animals. Changes in clinical pathology 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 6.2 IU greater for dogs receiving placebo.

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

HOW SUPPLIED: Rimadyl capsules are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per capsule. Each net site is packaged in bottles containing 30, 60, or 100 capsules, or blister packs containing 4 capsules.

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For a copy of the Minimal Safety Data Sheet (MSDS) call 1-800-729-3600. To report adverse reactions call Pfizer Animal Health at 1-800-368-8289.

NADA #141-024, Approved by FDA



Distributed by:
Pfizer Animal Health
Div. of Pfizer Inc
NY, NY 10017

LOT
Exp

820556000

RIMADYL[®]
(carprofen)

100 mg

180 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)



FPO: UPC

LOT
EXP

820555000

RIMADYL®
(carprofen)

100 mg

60 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)

Pfizer

FPO - UPC

EXP
LOT

0000550000

RIMADYL®
(carprofen)

100 mg

30 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
and-inflammatory drug
(NADA #141-053
Approved by FDA)



FFO - UPC



LOT
Exp

820554000

RIMADYL®
(carprofen)

75 mg

180 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

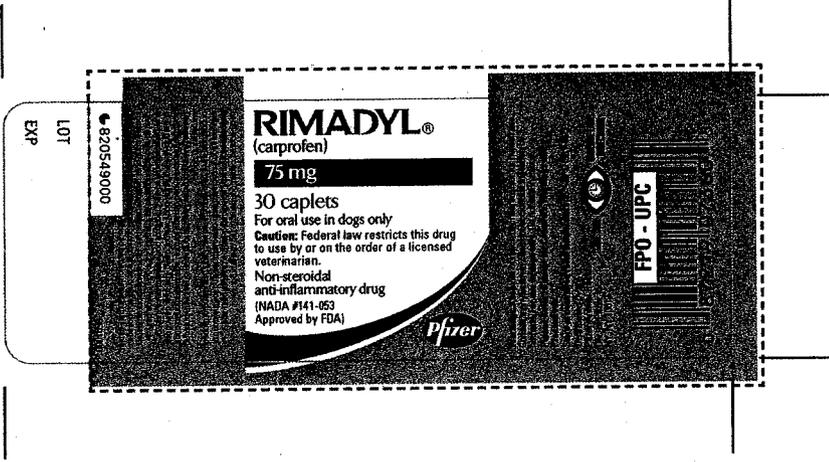
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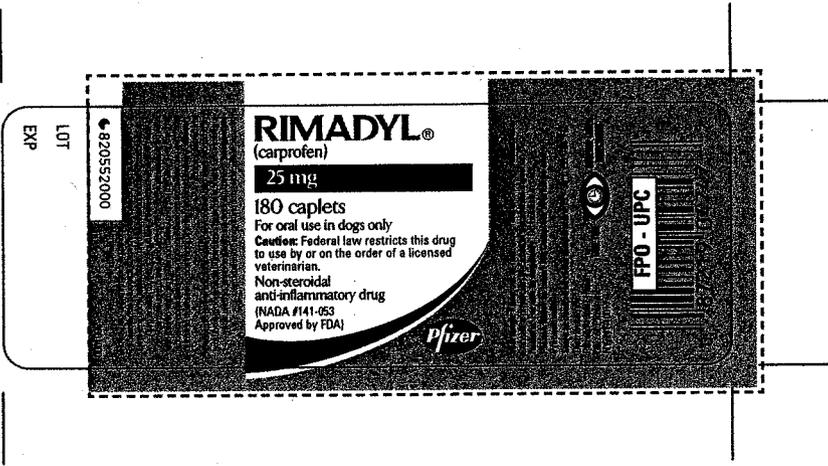
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LOT
EXP

820851000

RIMADYL®
(carprofen)

25 mg

60 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)

Pfizer

PPO - UPC

LOT
EXP

820548000

RIMADYL®

(carprofen)

25 mg

30 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)

Pfizer

FPO - UPC