



RIMADYL Rewards Program: Healthy Rewards for You and Your Dog

Healthy Rewards

The RIMADYL® (carprofen) Rewards Program is a rewarding way to partner with your veterinarian to ensure the health and well-being of your dog. It's also a great way to help you provide the long-term care your dog needs.

What does healthy rewards mean? It means that you can use your Rewards points towards ANY expense at your veterinary clinic including diagnostics and annual exams.

EARN DOLLARS WITH YOUR LOVING CARE.

As you continue to care for your dog with RIMADYL, the #1 pain medication prescribed by veterinarians,¹ you'll accumulate reward points based on the amount of RIMADYL you purchase. These Reward points translate into dollar amounts you can spend exclusively at your veterinary clinic to offset the cost for diagnostic tests, annual exams, additional RIMADYL or any other clinic expense.

Canine Arthritis

Just like in people, arthritis in dogs is a progressive, inflammatory condition that causes pain and also leads to irreversible joint damage. So what that means is that as arthritis gets worse, it becomes more difficult to treat.² However, unlike for people, many common human pain medications, like aspirin, are toxic to dogs. That's where RIMADYL comes in.

RIMADYL

RIMADYL was developed just for dogs, and is approved by the FDA for a once or twice-daily dosing with tasty chewable tablets or caplets. RIMADYL helps manage the pain and inflammation in your dog's joints.

Because dogs hide pain, it can sometimes be difficult to tell how much pain your dog is actually feeling. For other dogs, the signs are clear. The good news is, pain doesn't have to mean the end of your dog's active lifestyle. RIMADYL can help control pain and inflammation and revive the active spirit that lives inside your dog.

RIMADYL was the first pain medication for arthritis approved for dogs in the U.S. and has been trusted by veterinarians to manage inflammation and pain since 1997. Over 16 million dogs have been treated with RIMADYL making it the #1 pain medication prescribed by veterinarians.¹

**Every dog has his day. Make sure it's a good one.
Thank you for using RIMADYL.**

IMPORTANT SAFETY INFORMATION: RIMADYL is a non-steroidal anti-inflammatory medication available only by prescription through your veterinarian. As with other NSAID-class medications, signs of RIMADYL intolerance may include appetite loss, vomiting and diarrhea, which could indicate side effects involving the digestive tract, liver or kidneys. Some of these side effects may occur without warning and, in rare situations may be serious, resulting in hospitalization or even death. If these signs occur, discontinue RIMADYL therapy and consult your veterinarian. See the "Important Information for Dog Owners" section of the full prescribing information.

The RIMADYL Rewards Program Benefits You and Your Dog

- **Your dog gets the best care.** RIMADYL is the #1 pain medication prescribed by veterinarians. It can help control pain and inflammation and revive the active spirit that lives inside your dog.
- **Your veterinarian stays involved.** You partner with your veterinarian to ensure the health and well-being of your dog. By purchasing your RIMADYL at the veterinary clinic, you receive the expert advice only available through your veterinarian. Only your veterinarian knows the full health and medication history for your dog, and can work with you to determine the best course of treatment.
- **You earn Healthy Rewards.** As you continue to care for your dog with RIMADYL, you'll accumulate Reward points based on the amount of RIMADYL you purchase. These Reward points translate into dollar amounts that will be loaded on to your Rewards Card that you can use. As you continue to earn points, we continue to reload your Rewards Card with earned dollars. See program Terms and Conditions for details.
- **No rebate hassles.** You no longer have to keep up with rebate checks. The Reward dollars are automatically loaded onto your Rewards Card. And the reward is aligned to what you purchased.

MORE CONVENIENCE. MORE FEATURES.

Although canine arthritis can be painful, participating in the Rewards Program doesn't have to be. We've provided many easy ways to reap the rewards of this program.

In addition to submitting proof of purchase via mail or online, the RIMADYL Rewards Program has a **free mobile app** where you can create your dog's profile (upload a photo!), upload your qualifying RIMADYL proof of purchase (receipts from your veterinary clinic), check your account balance and sign up to receive dosage and refill reminders.



To download this free app, please visit the iTunes store.



Reaping the Rewards is Easy

THE RIMADYL REWARDS PROGRAM:

1. Purchase RIMADYL through your veterinarian to help your dog with long-term care for the pain and inflammation associated with his or her arthritis.
2. Every time you purchase RIMADYL, submit your veterinary receipts as proof-of-purchase. Receipts must state the date RIMADYL was purchased and be from a veterinary clinic or an authorized home delivery company.
3. Your points accumulate, and when you reach 200 points, a RIMADYL Rewards Card loaded with your earned dollars gets mailed to you. **Hang on to that card!** Once you have your card, every time you submit your valid proof-of-purchase, dollars will be loaded on your card.
4. RIMADYL Rewards dollars can be used towards ANY expense at your veterinary clinic including diagnostics and annual exams.

When you purchase these RIMADYL Bottles*	You'll earn these points	Those points equal to these dollar amounts
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25mg x 30 Tablets	60	\$5.50
25mg x 60 Tablets	110	\$11.00
25mg x 180 Tablets	330	\$32.50
75mg x 30 Tablets	70	\$6.70
75mg x 60 Tablets	130	\$13.50
75mg x 180 Tablets	400	\$40.00
100mg x 30 Tablets	80	\$8.20
100mg x 60 Tablets	160	\$16.50
100mg x 180 Tablets	500	\$49.40

* RIMADYL Chewable Tablets and Caplets only.



Program Terms and Conditions:

RIMADYL REWARDS PROGRAM:

- Limit one (1) Rewards Card per household. Offer valid for purchases made after February 1st, 2012 or from date of dog's registration.
- Invoice is required to validate proof of purchase.
- Invoice may be sent via mail, fax, or by uploading a photo online. More information is available at www.rimadog.com
- Invoice must include the following information:
 - o Purchase of RIMADYL chewable tablets or caplets
 - o Dog's name
 - o Pet owner's name
 - o Veterinary clinic name or authorized home delivery company name
 - o Strength (mg) and size of bottle purchased (i.e., 25mg, 30 tablets)
 - o Receipts will not be accepted from online pharmacies or unauthorized home delivery companies.
- All proof-of-purchase invoices must be submitted within 1 (one) year of RIMADYL purchase.
- Minimum of 200 points per dog must be approved within 1 (one) year of initial proof of purchase submission for Rewards Card to be loaded with earned dollars the first time. After that, points will be loaded to the card with each valid proof-of-purchase provided.
- Purchases for multiple dogs cannot be combined to meet minimum point requirements. Maximum 3,360 points per dog per year.
- Rebate amount must be redeemed within 1 (one) year of last Rewards Card load or by card expiration date. Dollars not redeemed in that time are forfeited.
- Limit up to five (5) dogs per household.
- Users can monitor and track progress of proof-of-purchase approvals, balance inquiries and more by logging in to their MY ACCOUNT profile on www.rimadog.com.

Program can change at any time without notice. U.S. Residents Only.

¹ VetInsight Analytics, September 2010.

² Muir WW. Choosing and administering the right analgesia therapy. In: *Veterinary Pain Management*. Eds: Gaynor JS, Muir WW. Mosby 2002.

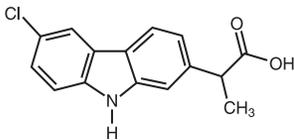
RIMADYL® (carprofen)

Caplets/Chewable Tablets
For oral use in dogs only

Sterile Injectable Solution 50 mg/mL

For subcutaneous use in dogs only

Non-steroidal, anti-inflammatory drug



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

DESCRIPTION: 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 carbazole, 6-chloro- α -methyl-9H-carbazole-2-acetic acid. The empirical formula is $C_{17}H_{12}ClNO_2$ and the molecular weight 273.72. The chemical structure of carprofen is shown above. Carprofen is a white, crystalline compound. It is freely soluble in ethanol, but practically insoluble in water at 25°C.

Rimadyl Injectable is a sterile solution containing carprofen. Each mL of Rimadyl Injectable contains 50.0 mg carprofen, 30.0 mg arginine, 88.5 mg glycolic acid, 169.0 mg leucine, 10.0 mg benzyl alcohol, 6.17 mg sodium hydroxide, with additional sodium hydroxide and hydrochloric acid as needed to adjust pH, and water for injection.

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: 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.² In an *in vitro* study using canine cell cultures, carprofen demonstrated selective inhibition of COX-2 versus COX-1.³ 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.

Several studies have demonstrated that carprofen has modulatory effects on both humoral and cellular immune responses.^{4,5} Data also indicate that carprofen inhibits the production of osteocalcin-activating factor (OAF), PGE₁, and PGE₂ by its inhibitory effect in 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.⁶ 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. Rimadyl is more than 99% bound to plasma protein and exhibits a very small volume of distribution.

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

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

INDICATIONS: 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 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 hematology 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.^{7,8} 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.^{11,15} 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. Concomitant use of Rimadyl with other anti-inflammatory drugs, such as other NSAIDs or corticosteroids, should be avoided because of the potential increase of adverse reactions, including gastrointestinal ulcerations and/or perforations. Sensitivity to drug-associated adverse reactions varies with the individual patient. Dogs that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Rimadyl treatment was not associated with renal toxicity or gastrointestinal ulceration in well-controlled safety studies of up to 10 times the dose in healthy dogs. As with any parenterally injected product, good hygienic procedures should be used when administering Rimadyl Injectable.

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, in pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. Safety has not been established for IV or IM administration. Studies to determine the activity of 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.¹⁶ It is suggested to use different sites for additional injections. 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.

Due to the palatable nature of Rimadyl chewable tablets, store out of reach of dogs in a secured location. Severe adverse reactions may occur if large quantities of tablets are ingested. If you suspect your dog has consumed Rimadyl chewable tablets above the labeled dose, please call your veterinarian for immediate assistance and notify Pfizer Animal Health (1-800-366-5288).

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 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.

ADVERSE REACTIONS: During investigational studies for the caplet formulation 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 caplet- and placebo-treated dogs. Incidences of the following were observed in both groups: vomiting (4%), diarrhea (4%), changes in appetite (3%), lethargy (1.4%), behavioral changes (1%), and constipation (0.3%). The product vehicle served as control.

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

Percentage of Dogs with Abnormal Health Observations Reported in Clinical Field Study (2 mg/lb once daily)		
Observation	Rimadyl (n=129)	Placebo (n=132)
Inappetence	1.6	1.5
Vomiting	3.1	3.8
Diarrhea/Soft stool	3.1	3.5
Behavior change	0.8	0.8
Dermatitis	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 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	13.4
Diarrhea/Soft stool	6.1	6.0
Ocular discharge	2.7	0
Inappetence	1.4	0
Dermatitis/Skin lesion	0.7	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.

During investigational studies for the chewable tablet formulation, gastrointestinal signs were observed in some dogs. These signs included vomiting and soft stools.

There were no serious adverse events reported during clinical field studies for the injectable formulation. The following categories of abnormal health observations were reported. The product vehicle served as control.

Percentage of Dogs with Abnormal Health Observations Reported in Clinical Field Studies with the Injectable

Observation*	Rimadyl (n=168)	Placebo (n=163)
Vomiting	10.1	9.2
Diarrhea/soft stool	7.4	3.7
Dermatitis	0.6	1.2
Dysrhythmia	0.6	0.6
Swelling	0	1.2
Dehiscence	1.2	0
WBC increase	13.7	6.7

* 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 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.

In rare situations, injection site reactions including necrosis, abscess and seroma formation, and granulomas have been reported with the injectable formulation.

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.

DOSE AND ADMINISTRATION: Always provide Client Information Sheet with prescription. Carefully consider the potential benefits and risk of Rimadyl and other treatment options before deciding to use Rimadyl. Use the lowest effective dose for the shortest duration consistent with individual response. 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 surgery. Rimadyl tablets are scored and dosage should be calculated in half-tablet increments. Tablets can be halved by placing the tablet on a hard surface and pressing down on both sides of the score. Rimadyl chewable tablets are palatable and willingly consumed by most dogs when offered by the owner. Therefore, they may be fed by hand or placed on food. Care should be taken to ensure that the dog consumes the complete dose.

The recommended dosage for subcutaneous administration to dogs is 2 mg/lb (4.4 mg/kg) of body weight daily. The total daily dose may be administered as either 2 mg/lb of body weight once daily or divided and administered as 1 mg/lb (2.2 mg/kg) twice daily. For control of postoperative pain, administer approximately 2 hours before the procedure.

PALATABILITY: A controlled palatability study was conducted which demonstrated that Rimadyl chewable tablets were readily accepted and consumed on first offering by a majority of dogs.

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 7 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, when divided and administered at 1 mg/lb twice daily. In these 2 field studies, dogs diagnosed with osteoarthritis showed statistically significant overall improvement based on lameness evaluations by the veterinarian and owner observations when administered Rimadyl at labeled doses.

Based upon the blood level comparison between subcutaneous and oral administration, Rimadyl effectiveness for osteoarthritis after dorso-scapular subcutaneous and oral administration should be similar, although there may be a slight delay in the onset of relief after subcutaneous injection.

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 presented for ovariohysterectomy, cruciate repair and anal surgeries 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 reduction 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 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 (2.26 g/dL) than each of 2 placebo control groups (2.88 and 2.93 g/dL, respectively). Three incidents of black or bloody stool were observed in 1 dog. Five of 8 dogs exhibited reddened areas of duodenal mucosa on gross pathologic examination. Histologic exam of these areas revealed no evidence of ulceration, but did show minimal congestion of the lamina propria in 2 of the 5 dogs.

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

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

Clinical field studies were conducted with 549 dogs of different breeds at the recommended oral doses for 14 days (297 dogs were included in a study evaluating 1 mg/lb twice daily and 252 dogs were included in a separate study evaluating 2 mg/lb once daily). In both studies the drug was clinically well tolerated and the incidence of clinical adverse reactions for Rimadyl-treated animals was no higher than placebo-treated animals (placebo contained inactive ingredients found in Rimadyl). 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 Rimadyl 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 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 297 dogs of different breeds undergoing orthopedic or soft-tissue surgery. Dogs were administered 2 mg/lb of Rimadyl 2 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 observation 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 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 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.

Clinical field studies on the use of Rimadyl Injectable were conducted on 331 dogs undergoing orthopedic or soft tissue surgery. Dogs were administered 2 mg/lb of Rimadyl subcutaneously 2 hours prior to surgery and once daily thereafter, 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 hematopoietic, renal, hepatic, and clotting function were not clinically significant. The mean post-treatment serum ALT values were 8.4 IU and 7.0 IU less than pre-treatment values for dogs receiving Rimadyl and placebo, respectively. The mean post-treatment AST values were 1.5 IU and 0.7 IU greater for dogs receiving Rimadyl and placebo, respectively.

STORAGE: Store tablets at controlled room temperature 15°–30°C (59°–86°F). Store injectable under refrigeration 2°–8°C (36°–46°F). Once broached, product may be stored at temperatures up to 25°C (77°F) for 28 days.

HOW SUPPLIED: Rimadyl caplets and chewable tablets are scored, and contain 25 mg, 75 mg, or 100 mg of carprofen per caplet or tablet. Each caplet size is packaged in bottles containing 30, 60, or 180 caplets, or blister packs containing 4 caplets. Each chewable tablet size is packaged in bottles containing 7, 30, 60, or 180 tablets. Rimadyl Injectable is supplied in 20-mL, amber, glass, sterile, multi-dose vials.

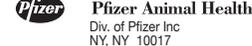
REFERENCES:

- Baruth H, et al: *Anti-Inflammatory and Anti-Rheumatic Drugs*. Vol II, Newer Anti-Inflammatory Drugs, Rainsford KD, ed. CRC Press, Boca Raton, p. 33, 1986.
- Vane JR, Botting RM: Mechanism of action of anti-inflammatory drugs. *Scand J Rheumatol* 25:102, pp. 9–21, 1996.
- 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.
- Ricketts AP, Lundy KM, Seibel SB: Evaluation of selective inhibition of canine cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs. *Am J Vet Res* 58:11, pp. 1441–1446, November 1998.
- Coupeens JL, et al: Non-steroidal anti-inflammatory agents inhibit the synthesis of IgM rheumatoid factor in vitro. *Lancet* 1:528, 1982.
- Coupeens JL, et al: Endogenous prostaglandin E₂ enhances polyclonal immunoglobulin production by ionically inhibited T suppressor cell activity. *Cell Immunol* 70:41, 1982.
- Schleimer RP, et al: The effects of prostaglandin synthesis inhibition on the immune response. *Immunopharmacology* 3:205, 1981.
- Leung KH, et al: Modulation of the development of cell mediated immunity: Possible roles of the products of cyclooxygenase and lipoygenase pathways of arachidonic acid metabolism. *Int J Immunopharmacol* 4:195, 1992.
- Voit BC: Immunoregulatory activity of cultured-induced suppressor macrophages. *Cell Immunol* 72:14, 1982.
- Schmitz M, et al: Biopharmaceutical evaluation of carprofen following single intravenous, oral, and rectal doses in dogs. *Biopharm Drug Dispos* 11(7):585, 1990.
- Kore AM: Toxicology of nonsteroidal anti-inflammatory drugs. *Veterinary Clinics of North America, Small Animal Practice* 20, March 1990.
- Birns SH: Pathogenesis and pathophysiology of ischemic injury in cases of acute renal failure. *Compend For Cont Ed* 16, January 1994.
- Boothe DM: Prostaglandins: Physiology and clinical implications. *Compend For Cont Ed* 6:11, November 1984.
- Rubin SJ: Nonsteroidal anti-inflammatory drugs, prostaglandins, and the kidney. *JAVMA* 188:9, May 1986.
- Ko CH, Lange DN, Mandsgager RE, et al: Effects of butorphanol and carprofen on the minimal alveolar concentration of isoflurane in dogs. *JAVMA* 217:1025–1028, 2000.

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