Are you administering NSAIDs at the appropriate dose and duration to dogs with osteoarthritis?

- Prospective, Randomized, Blinded Study 59 client-owned dogs with pain or impaired mobility due to osteoarthritis
- **MDG:** Maintenance Dose Group, meloxicam at 0.2 mg/kg Day 1; then 0.1 mg/kg for remainder of study; N=29
- **RDG:** Reduced Dose Group, meloxicam at 0.2 mg/kg Day 1; then 0.1 mg/kg for 13 days; then reduced by 15 % q 14 days; N=30
- **Study Duration:** 112 days
- **Primary Outcome:** Number of dogs that dropped out of study because of insufficient pain control as assessed by owners. Additional outcome measures were owner-assessed pain control (Helsinki Chronic Pain Index, Canine Brief Pain Inventory), Activity Monitors, Percent Body Weight Distribution to the index limb
- **Secondary Outcomes:** Client-Specific Outcome Measure, Adverse Events
- Significantly more dogs dropped out of the RDG (n=13) than MDG (N=6)
- 57% of dogs in the RDG tolerated gradual dose reduction
- Adverse event rate was low and similar between the two groups
Kaplan Meier plot of cumulative proportion of dogs for each group remaining in the study. Dogs in the Reduced Dose Group (RDG) dropped out of the study at a faster rate than dogs in the Maintained Dose Group (MDG) (P .035)

- Dose reduction is a less effective means of pain control compared with maintained dosing.

- Successful dose reduction can be employed, but appears to be dependent on individual dog; optimal strategy for dose reduction requires additional study.
THE PROVEN EFFECTIVE RIMADYL DOSE FOR DOGS WITH OSTEOARTHRITIS IS 2 mg/lb/day\textsuperscript{1}

**RIMADYL Study.** Laboratory study evaluating the effects of RIMADYL in dogs with surgically induced osteoarthritis.

**Doses:** 0 (placebo) 1, 2, 3 or 4 mg/lb/day of RIMADYL.

Dogs treated with RIMADYL at 2, 3, 4 mg/lb/day, but not dogs treated with 1 mg/lb/day, had significantly greater range of motion than placebo control group.

The label dose of RIMADYL (2 mg/lb/day, 4.4 mg/kg/day) is the lowest effective dose for relief of pain and inflammation associated with canine osteoarthritis.
**DETERMINING THE RIGHT DURATION OF TREATMENT**

**STUDY**


**STUDY DESIGN**

- Systematic Review, 15 peer-reviewed papers evaluating the efficacy and/or safety of NSAIDs used for > 28 days in the treatment of canine osteoarthritis

**ASSESSMENT PARAMETERS**

- Strength of scientific data rated on a modified criteria produced by the FDA
- 10 studies included carprofen, 4 studies included meloxicam, 3 studies included firocoxib, 3 studies included etodolac, 1 study included deracoxib
- 6 of 7 studies indicated benefit of long-term treatment (>28 days) over short-term treatment with NSAIDs
- 14 studies evaluating safety found no correlation between study length and experimental adverse event rate

**RESULTS**

The current evidence suggests that there is a clinical benefit of longer-term NSAID use for dogs with chronic osteoarthritis, and this is associated with a low risk of adverse events.

- **Prospective Clinical Trial**
  - 110 client-owned dogs with clinical signs of chronic osteoarthritis
  - Received RIMADYL, 4 mg/kg PO daily for 120 days
  - Assessed day 0, 5, 30, 60, 90, 120

- **Veterinary:** VAS scores of osteoarthritis (4 parameters)
- **Pet Owner:** Grade of osteoarthritis (7 parameters)
- **Blood work days:** 0, 60 and 120

- 88% compliance throughout study
- Dogs with a response had a steady increase from Day 5 (12%) to Day 120 (74%)
- 98% of dogs showed improvement; 2% had no improvement; 1 dog dropped out of study due to lack of efficacy
- 5% of dogs had adverse events related to RIMADYL; 2 dogs withdrawn from study, recovered with treatment

**DETERMINING THE RIGHT DURATION OF TREATMENT**
The results of this study clearly demonstrate that the long-term administration of carprofen provides a steadily increasing improvement of clinical signs of osteoarthritis in dogs and does not result in an increased incidence of suspected adverse reactions.

Patients removed from the study for reasons other than treatment failure were omitted from scheduled visits following removal; patients removed from the study for treatment failure were carried over following scheduled visits until study end, i.e., Day 120 visit. (Number and percentage of Treatment Failure are therefore cumulative.)

Number of dogs still involved in the study: 110 on Day 5; 109 on Day 30; 106 on Day 60; 104 on Day 90 and 100 on Day 120
EVOLUTION OVER TIME OF THE 4 CLINICAL PARAMETERS SCORED BY INVESTIGATORS

Day of Study

0 5 10 15 20 25 30 35 40 45 50 55 60

VAS Score (mm)

0 5 10 15 20 25 30 35 40 45 50 55 60

Overall severity of the condition
Lameness
Limitation of joint movements
Pain of movement
Important Safety Information: As with other NSAIDs, rare but serious side effects involving the digestive system, kidneys, or liver may occur. Regular monitoring is required for pets on medication. Pet owners should be advised to discontinue RIMADYL therapy if side effects occur and to contact their veterinarian. Refer to the full prescribing information for complete details.


KEY TAKE-AWAYS

• RIMADYL at 2mg/lb/day (4.4 mg/kg/day) is the proven lowest effective dose.¹

• The long-term administration of RIMADYL provides a steadily increasing improvement in the clinical signs of osteoarthritis in dogs.²

• Long-term treatment with RIMADYL does not result in increase incidence of suspected adverse events.²

RIMADYL®
(carprofen)

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¹ RIMADYL (carprofen) Freedom of Information Summary NADA 141-053, 1996.
There were no serious adverse events reported during clinical field studies for the injectable formulation. The following categories of abnormal adverse reactions were reported.

<table>
<thead>
<tr>
<th>Observation*</th>
<th>Rimadyl® (n=165)</th>
<th>Placebo (n=167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>3.5%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.1%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1.1%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Pelvic pain</td>
<td>1.1%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Hematuria</td>
<td>1.1%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Wound drainage</td>
<td>1.1%</td>
<td>0%</td>
</tr>
<tr>
<td>Urinary tract disease</td>
<td>1.3%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0.6%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Ocular disease</td>
<td>2.7%</td>
<td>0%</td>
</tr>
<tr>
<td>Bilirubinuria</td>
<td>16.3%</td>
<td>12.1%</td>
</tr>
<tr>
<td>Diarrhea/Soft stool</td>
<td>4.5%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Inappetence</td>
<td>1.5%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

In rare situations, death has been associated with some of the adverse reactions listed above. In all studies, owners were advised of the potential for side effects and the need to discontinue therapy in cases of unacceptable reactions by humans. For use in dogs only. Do not use in cats.

CONTRAINDICATIONS: Rimadyl® should not be used in dogs exhibiting previous hypersensitivity to carprofen or in dogs with a history of gastrointestinal ulceration. For use in dogs only. Do not use in cats.

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

Information on adverse experiences that are not included in the label or have been reported infrequently: in clinical studies with carprofen, occasional reports of hypocalcemia and hyperkalemia were noted. No consistent differences in the incidence or magnitude of these laboratory changes were noted between the two groups (active vs. placebo).

The empirical formula is C15H12ClNO2 and the molecular weight is 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.

Carprofen is an aryloxypropionic acid derivative with a chemical and pharmacological structure similar to that of aspirin and the other non-steroidal anti-inflammatory drugs (NSAIDs). Carprofen is used for the management of arthritis-related pain and inflammation in cats and dogs.

Carprofen is a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class that includes ibuprofen, naproxen, and flurbiprofen. Carprofen is a non-salicylate, non-steroidal, non-opioid anti-inflammatory agent with analgesic and anti-inflammatory activity.

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The mechanism of action of carprofen, like that of other NSAIDs, is believed to involve the inhibition of cyclooxygenase (COX).

Two unique cyclooxygenase isozymes are identified, cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). COX-1 is a constitutively expressed enzyme that is required for platelet function and is responsible for maintaining normal gastrointestinal function. The inducible cyclooxygenase, COX-2, generates prostaglandins in response to an inflammatory stimulus. COX-2 is induced in cells of the macrophage lineage, which are responsible for inflammation. The selectivity of a particular NSAID for COX-2 is of critical importance to its activity and potential for toxicity. In vitro studies using human colon carcinoma cells have demonstrated that carprofen selectively inhibits COX-2.

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