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## Monitoring Dogs on NSAIDs

You have asked...

*How do I monitor dogs receiving long-term nonsteroidal anti-inflammatory drug therapy?*

The expert says...

**T**he number of senior dogs is growing, and an estimated 25% of them will develop arthritis. Given this statistic and the growing interest in pain management for pets, NSAIDs are one of the most commonly prescribed veterinary medicines for long-term use.

The number of adverse drug events associated with canine NSAID use reported to the U.S. Food and Drug Administration Center for Veterinary Medicine greatly exceeds that reported for other drugs used in companion animals.<sup>1</sup> However, because so many dogs are prescribed NSAIDs, the actual incidence of untoward side effects would appear to be very low. Pfizer Animal Health has reported that the approximate incidence of adverse drug events is 0.009% in an estimated 1.5 million dogs treated with carprofen (data on file, Pfizer Animal Health).

### Adverse Effects & Causes

The most common adverse effects of NSAID use, in order of the number reported, involve the gastrointestinal, hepatic, renal, and hematologic systems. The most commonly affected group is dogs 10 to 15 years old, followed by 6- to 10-year-old dogs.<sup>1</sup>

Many adverse drug events occur when the drug is used at doses higher than those approved, when another NSAID (including aspirin) or corticosteroids are used concurrently or in close temporal association, or when concurrent disease is present.<sup>2</sup> However, adverse effects can occur in dogs with no obvious risk factors and when the drug is used correctly.<sup>2,3</sup> Hepatocellular toxicosis associated with this class of drug is thought to be idiosyncratic.<sup>3</sup>

### Monitoring: What to Do

Despite our knowledge of the mode of action and known side effects of NSAIDs, there are few

NSAID = nonsteroidal antiinflammatory drug

scientific data on how to monitor patients receiving long-term therapy so that problems can be caught early, before permanent organ damage occurs. Monitoring these patients includes testing for abnormalities before treatment begins and at intervals during treatment.

All manufacturers of NSAIDs recommend screening animals (by physical examination and hematologic and clinical chemistry evaluation) before starting treatment, but the best frequency of such screening is unknown. In one study, only 2 of 15 dogs that sustained serious side effects after administration of an NSAID underwent laboratory tests before the drug was prescribed for long-term use.<sup>2</sup> Monitoring the dog for clinical side effects by both the veterinarian and an *informed* owner is invaluable.<sup>4</sup>

### Veterinary Monitoring

Because the most common adverse effects of NSAIDs involve the gastrointestinal, renal, hepatic, and hematologic systems, it is logical to test for impairment in these organs. Tests for ALP, ALT, and AST (to evaluate liver insult) and tests for BUN and creatinine (to assess renal function) are recommended. A commercial NSAID monitoring panel (VetTest Chemistry Analyzer, [www.idexx.com](http://www.idexx.com)) is available for convenient monitoring.

#### *What do abnormalities or changes in blood chemistries mean, and what values are cause for concern?*

Gastrointestinal bleeding should be suspected if the hematocrit falls during treatment, and an increase in BUN level may also suggest bleeding in the gut. Liver enzymes may be induced by long-term drug therapy, but a 3- to 4-fold increase in hepatic enzymes above the normal range or from baseline values suggests hepatotoxicity.

If liver enzyme values return to baseline after discontinuation of the drug, a link between treatment and hepatic impairment is very likely. If the relevance of liver enzyme results is uncer-

tain, more definitive tests of hepatic function, such as bile acid assays, can be performed.

Keep in mind, though, that elevated hepatic enzyme levels are not necessarily a risk factor for hepatopathy, and mild changes in BUN and creatinine levels do not always preclude the use of NSAIDs.

#### *How often should patients be monitored?*

According to data from the FDA Center for Veterinary Medicine, most adverse drug events occur between days 14 and 30 (range, 3–90 days) after the start of treatment.<sup>1</sup> Thus, blood analysis performed before treatment and then at 2 to 4 weeks seems sensible. Thereafter there is no consensus on how often to screen, but it would be prudent to screen dogs older than 10 years every 3 months and younger dogs every 6 to 12 months. Screening should include but not be restricted to ALT, AST, ALP, BUN, and creatinine.

### The Owner's Watch

The decision to initiate treatment will be based on discussion with the owner and an analysis of the risks and benefits of treatment. Educating owners about the early signs of potential problems is one of the most important ways to prevent them. Clients should be advised to stop administering the NSAID and call the veterinarian if they notice any changes in their pets, such as inappetence, vomiting, diarrhea, lethargy, or bloody feces. After consultation and perhaps further diagnostics, a decision can be made about whether to continue treatment. The key is to catch problems early and err on the side of caution.

### Event Reporting

All adverse drug events should be reported to the relevant pharmaceutical company and/or the FDA Center for Veterinary Medicine so that we can learn more about why they occur. ■

**See Aids & Resources, back page, for references, contacts, and appendices.**

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ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; NSAID = nonsteroidal antiinflammatory drug