DERACOXIB

• Manages pain and inflammation associated with osteoarthritis in dogs
• Manages postoperative pain from orthopedic surgery in dogs

Deracoxib is the newest member of the coxib class of nonnarcotic, nonsteroidal, selective cyclooxygenase (COX)-2 inhibiting antiinflammatory drugs. This drug class, which includes carprofen and etodolac, is approved for managing pain and inflammation associated with osteoarthritis in dogs. Until recently, there were no oral agents approved for controlling postoperative pain. Deracoxib was approved by the FDA in August 2002 for managing postoperative pain from orthopedic surgery in dogs and in February 2003 for managing chronic pain in dogs.

PHARMACOLOGY

Deracoxib has a mechanism of action similar to traditional NSAIDs in that its effect comes from the inhibition of the COX-2 enzyme. The COX-2 enzyme is expressed during times of tissue damage and contributes to the transmission of pain and inflammation. Deracoxib differs from traditional NSAIDs in its lack of inhibition of the COX-1 enzyme. This enzyme is present in many tissues and serves to produce prostanoids responsible for the homeostatic balance of various physiologic functions. COX-1 is required for normal platelet function, sodium homeostasis in the kidneys, and protection of the gastrointestinal (GI) mucosa.

The COX-2 selectivity of a drug can be evaluated by its median inhibitory concentration (IC$_{50}$), which is the concentration of the drug that inhibits an enzyme (COX-1 or COX-2) by 50%. By calculating an IC$_{50}$ ratio, it is possible to compare drugs within a test system (one study in the same species). A higher COX-1:COX-2 ratio indicates a more favorable result and higher selectivity for inhibiting the COX-2 enzyme. The IC$_{50}$ ratio for deracoxib is 1,275.

PHARMACOKINETICS

The plasma terminal elimination half-life for deracoxib is around 3 hours. However, clinical effectiveness is observed for a longer duration, thereby allowing once-daily dosing. Nonlinear elimination kinetics are seen with dosages exceeding 8 mg/kg/day PO. This is the estimated dosage at which competitive inhibition of the COX-1 enzyme is likely to occur. The route of elimination for this drug is through hepatic biotransformation. This produces four major metabolites; two are characterized as products of oxidation and o-demethylation. Most of the ingested deracoxib is excreted in the feces as parent drug or metabolite, and a small amount of metabolite may be excreted through the urine.

INDICATIONS

NSAIDs are widely used in both human and veterinary medicine for controlling acute and chronic pain. Deracoxib is an NSAID approved for use in dogs heavier than 4 lb to control postoperative pain and inflammation associated with orthopedic surgery. The current indication is for short-term use up to 7 days as needed. Several studies have evaluated deracoxib as long-term therapy for osteoarthritis, and the relevant data have been submitted to the FDA for approval of this indication. These include safety studies evaluating up to 10 times the recommended long-term dosage for 6 months and a 6-week study evaluating the tolerability and effectiveness of deracoxib.

CAUTIONS

Dogs with a known hypersensitivity to deracoxib should not receive this medication. This medication is not in-
Deracoxib is used to control pain and inflammation following your dog’s surgery.

- Deracoxib should be given to your dog only at the dose prescribed by your veterinarian.
- Tablets should be given orally, preferably with food.
- Call your veterinarian if your dog shows abnormal signs while receiving deracoxib (e.g., vomiting, diarrhea, change in stool color, change in drinking or urination, decrease in appetite, bruising on gums and groin).
- Tell your veterinarian about any past adverse drug reactions to aspirin or other NSAIDs that your pet has had.
- Tell your veterinarian about any current or past medical problems (especially regarding the kidneys, liver, or digestive tract) with your dog.

### Client Counseling Information

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>$T_{\text{max}}$</td>
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<tr>
<td>Oral bioavailability (F)</td>
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<tr>
<td>Terminal elimination half-life</td>
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<tr>
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<tr>
<td>Protein binding</td>
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$^{a}$Values were obtained following a single 2.35-mg/kg dose.
$^{b}$Estimates following IV administration of the drug as an aqueous solution.
$^{c}$Based on a dose of 2 mg/kg.
$^{d}$Based on in vitro plasma concentrations of 0.1, 0.3, 1, 3, and 10 µg/ml.

**Table 1. Pharmacokinetics of Deracoxib**

ACUTE TOXICITY

Because of the selectivity toward the COX-2 enzyme, there are fewer side effects with deracoxib than with traditional NSAIDs. In a field study of 207 dogs (43 breeds) 1 to 15 years of age, the most common side effects were vomiting and incisional drainage, each occurring in 11 dogs compared with six in the placebo group. Additional side effects seen during the study were rare but included diarrhea, hematochezia, skin lesions at sites other than the incision, otitis externa, phlebitis, positive joint culture, hematuria, splenomegaly, and hepatomegaly. In other studies, increased GI side effects, resembling those of traditional NSAIDs, were seen at dosages higher than 8 mg/kg/day PO, resulting from inhibition of the COX-1 enzyme at such high doses. Deracoxib was well tolerated by most dogs at a dosage of 3 to 4 mg/kg/day PO. As a class, NSAIDs can cause GI and renal toxicity. Dogs that are dehydrated; are currently receiving diuretic therapy; or have existing renal, cardiovascular, or hepatic dysfunction are at highest risk for renal problems. At the recommended therapeutic dosages, no toxicities were shown to be clinically significant in safety studies of deracoxib. In one study, there was a dose-dependent trend toward increased levels of blood urea nitrogen in dogs given more than 6 mg/kg/day PO. An additional study showed that overdoses of deracoxib could lead to serious adverse events as with other NSAIDs. At doses of 25, 50, and 100 mg/kg, weight loss, vomiting, melena, and GI ulcers and erosions were seen, and effects were worsened by higher doses.

**DRUG INTERACTIONS**

In field studies, deracoxib has been safely used along with other common medications, including heartworm preventatives, anthelmintics, anesthetics, preanesthetics, and antibiotics. A non–NSAID-type drug is recommended if additional pain medication is needed during deracoxib therapy. Administration of other potentially nephrotoxic drugs during treatment with deracoxib should be approached with extreme caution.

**DOSE AND ADMINISTRATION**

The total daily dose of deracoxib for postoperative orthopedic pain is 3 to 4 mg/kg PO in a single dose as needed for 7 days. Although deracoxib can be administered with or without food, the bioavailability is greatest when it is taken with food. Deracoxib should be administered before the orthopedic procedure for optimal pain control. The tablets are scored; thus doses should be calculated in half-tablet increments. The safety profile of this drug allows for safe rounding...
to half tablets. The FDA recently approved a dosage of 1 to 2 mg/kg/day PO for long-term administration.

PREPARATIONS
Deracoxib is available under the brand name Deramaxx (Novartis Animal Health). The beef-flavored chewable tablets come in 25- and 100-mg strengths and are packaged in either 30- or 90-tablet bottles. The price is comparable to other veterinary-approved COX-2 inhibitors.

STORAGE AND HANDLING
Deracoxib tablets should be stored at room temperature (59°F to 86°F [15°C to 30°C]) out of the reach of children.

REFERENCES