

DERACOXIB Veterinary—Systemic[†]

A commonly used *brand name* for a veterinary-labeled product is *Deramaxx*.

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

[†]Not commercially available in Canada.

Category: Analgesic; anti-inflammatory (nonsteroidal).

Indications

Accepted

Inflammation, musculoskeletal (treatment)¹; or
Pain, musculoskeletal (treatment)¹—*Dogs*: Deracoxib is indicated for the control of pain and inflammation associated with osteoarthritis.^{R-1}
Inflammation, postoperative (treatment)¹; or
Pain, postoperative (treatment)¹—*Dogs*, at least 1.8 kilograms (4 pounds) of body weight: Deracoxib is indicated for the control of postoperative pain and inflammation associated with orthopedic surgery.^{R-1}

¹Not included in Canadian product labeling or product not commercially available in Canada.

Regulatory Considerations

U.S.—

Deracoxib is labeled for use only by or on the order of a licensed veterinarian.^{R-1}

Chemistry

Chemical group: Diaryl substituted pyrazole.^{R-1}

Chemical name: 4-[5-(3-difluoro-4-methoxyphenyl)-(difluoromethyl)-1H-pyrazole-1-yl] benzenesulfonamide.^{R-1}

Molecular formula: C₁₇H₁₄F₃N₃O₃S.^{R-1}

Molecular weight: 397.38.^{R-1}

Pharmacology/Pharmacokinetics

Mechanism of action/Effect: Anti-inflammatory—Deracoxib is a nonsteroidal anti-inflammatory drug (NSAID) of the coxib class.^{R-1}

It is a cyclooxygenase inhibitor and decreases the production of prostaglandin E₁ (PGE₁) and 6-keto prostaglandin F₁ (6-keto PGF₁).^{R-1}

¹Cyclooxygenase 1 (COX-1), present in most cells and tissues, is believed to produce cytoprotective prostaglandins active in maintaining normal gastrointestinal and renal function in mammals while COX-2 produces prostaglandins involved in inflammation.^{R-1}

In lipopolysaccharide-stimulated human whole blood, deracoxib was shown to inhibit COX-2-mediated PGE₂ production. Studies using cloned canine cyclooxygenase have shown that concentrations expected *in vivo* with administration of 2 to 4 mg per kg of body weight a day do not inhibit COX-1 *in vitro*.^{R-1; 6} However, it is not known how well this *in vitro* data relates to effects *in vivo*.^{R-1}; there is still much to be learned about the mechanisms of action for the NSAIDs.

Absorption: Oral bioavailability (F)—*Dogs*: With a single oral dose of 2.35 mg per kg of body weight (mg/kg), bioavailability is greater than 90%.^{R-1}

Distribution: Volume of distribution—*Dogs*: Approximately 1.5 liters per kg.^{R-1}

Protein binding: *Dogs*—Greater than 90% at *in vitro* plasma concentrations of 0.1 to 10 micrograms per milliliter.^{R-1}

Biotransformation: Deracoxib undergoes hepatic metabolism, producing four major metabolites.^{R-1}

Half-life: Terminal elimination—*Dogs:* Intravenous administration—
With a dose of 2 to 3 mg/kg: 3 hours.^{R-1}
With a dose of 20 mg/kg: 19 hours.^{R-1}

Note: Nonlinear elimination kinetics can be seen in dogs administered more than 8 mg/kg a day,^{R-1} causing deracoxib plasma concentration to rise higher than would be expected if proportional to the increasing dose.^{R-3} Competitive inhibition of COX-1 can occur when doses higher than recommended are administered, leading to increased risk of toxicity.^{R-1; 3}

Time to peak serum concentration: *Dogs*—With an oral dose of 2.35 mg/kg: 2 hours.^{R-1}

Elimination: Deracoxib is eliminated primarily in the feces as parent drug and metabolites. Only metabolites are distributed into the urine. There is great intersubject variability in drug metabolite profiles in feces and urine.^{R-1}

Clearance—*Dogs:*

With an intravenous dose of 2 mg/kg—Approximately 5 milliliters per minute per kilogram (mL/min/kg).^{R-1}

With an intravenous dose of 20 mg/kg—Approximately 1.7 mL/min/kg.^{R-1}

Precautions to Consider

Cross-sensitivity

There is a possibility that animals hypersensitive to sulfonamide medications could also be hypersensitive to deracoxib; however, there is no clinical evidence available to confirm it.^{R-1}

Species sensitivity

Cats: The use of deracoxib in cats is not recommended until more information about safety is available.^{R-7}

Reproduction/Pregnancy/Lactation

Dogs: The safety of administering deracoxib to dogs during breeding, pregnancy, or lactation has not been studied.^{R-1}

Pediatrics

Dogs: The safety of administering deracoxib to dogs younger than 4 months of age has not been studied.^{R-1}

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Anti-inflammatory drugs, nonsteroidal (NSAID) or
Corticosteroids

(administration of more than one NSAID or of a corticosteroid concurrently with a NSAID may greatly increase the risk of adverse effects)^{R-1; 2}

Nephrotoxic medications

(concurrent administration of NSAIDs with other medications associated with renal toxicity should be considered carefully before implementation)^{R-1}

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

- Cardiovascular disease^(R-1) or
- Hepatic dysfunction^(R-1) or
- Renal dysfunction^(R-1)
 - (because NSAIDs have been associated with renal toxicity in certain circumstances, risk to patients with cardiovascular, hepatic, or renal compromise may be increased; also, deracoxib is metabolized by the liver)
- Dehydration^(R-1)
 - (dehydration can increase the risk of renal toxicity)
- Gastrointestinal ulceration
 - (many NSAIDs are known to increase the risk of gastrointestinal disease, particularly ulceration;^(R-1) therefore, the presence of lesions before treatment may put an animal at risk of exacerbation or perforation)
- Hypersensitivity to deracoxib^(R-1)
 - (previous development of adverse effects from deracoxib may be an indication of increased risk of future sensitivity)

Patient monitoring

- The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):
- Blood chemistry and
 - Complete blood count (CBC) and
 - Urinalysis
 - (bloodwork and urinalysis pretreatment and periodically during treatment is recommended)^(R-1)
 - Physical exam
 - (a physical exam and history before treatment is recommended)^(R-1)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

Note: The side effects most commonly associated with nonsteroidal anti-inflammatory drugs are gastrointestinal. However, in a field study of the treatment of osteoarthritis pain and inflammation, the incidence of observed clinical adverse reactions, including diarrhea and vomiting, in dogs treated with the labeled dose of deracoxib (1 to 2 mg/kg a day for 43 days; 105 dogs) was similar to that of dogs administered placebo (104 dogs). There were no significant differences in complete blood count, serum chemistry, or buccal mucosal bleeding time results between deracoxib- and placebo-treated animals.^(R-1)

In a field study comparing the treatment of postoperative pain and inflammation with deracoxib (3 to 4 mg/kg a day from a day before surgery to 6 days after surgery) in a group of 105 dogs to treatment with placebo in another group of 102 dogs, the following abnormal health findings were recorded:

Incidence more frequent

Dogs

Diarrhea—reported in 6% of dogs treated with deracoxib for postoperative pain and 7% of placebo-treated dogs;^(R-1) **incision site lesion** (drainage, oozing)—10% of dogs treated with deracoxib and 6% of placebo-treated dogs;^(R-1) **vomiting**—reported in 10% of dogs treated with deracoxib and 6% of placebo-treated dogs^(R-1)

Incidence less frequent

Dogs

Hematochezia—4% of dogs treated with deracoxib; **hematuria**—2% of dogs treated with deracoxib; **otitis externa**—2% of dogs treated with deracoxib; **skin lesions, nonincisional**—2% of dogs treated with deracoxib^(R-1)

Incidence rare—<1% of animals treated with deracoxib

Dogs

Conjunctivitis—2% of dogs treated with placebo; **hepatomegaly; phlebitis; positive joint culture; splenomegaly**

Overdose

For more information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Note: Nonlinear elimination kinetics can be seen in dogs administered more than 8 mg per kg of body weight (mg/kg) a day,^{R-1} causing deracoxib plasma concentration to rise higher than would be expected if proportional to the increasing dose.^{R-3} Competitive inhibition of COX-1 can occur when doses higher than recommended are administered, leading to increased risk of toxicity.^{R-1; 3}

Dogs

With a dose of 6 to 10 mg/kg a day for 6 months, the following were reported during the treatment period:^{R-1}

Elevated blood urea nitrogen (BUN); hyposthenuria; polyuria; renal changes

Note: Elevated blood urea nitrogen (BUN, mean 30, 35.3, and 48.2 mg per decaliter for dogs given 6, 8, or 10 mg/kg a day, respectively) was recorded at the end of six months in all dogs administered deracoxib in this dosage range. Two of ten dogs given 6 mg/kg a day developed hyposthenuria and polyuria. All dogs had serum creatinine, serum electrolyte, and urine sediment within normal range. In some dogs, renal histopathology revealed a dose-dependent focal renal tubular degeneration/regeneration and, in a few dogs given the highest doses, focal renal papillary necrosis was seen.^{R-1; 4}

With a dose of 16.92 mg/kg a day for 7 days, the following were reported in the one dog treated:^{R-1}

Decreased appetite; diarrhea; increased water intake; vomiting

Note: Signs resolved within 3 days of ending treatment.

With a dose of 10 to 100 mg/kg a day for 14 days, the following were reported during the treatment period:^{R-1}

Gastrointestinal irritation or ulceration (decreased body weight, melena, vomiting)

Note: In this study, the number and severity of *gastrointestinal lesions* seen in dogs increased with increasing dose. With the lowest dose, moderate diffuse congestion of gut associated lymphoid tissue and erosions or ulcers were observed in the jejunum while no change in body weight was recorded.^{R-1} Most dogs that received a dose ≥ 25 mg/kg developed melena, sporadic vomiting, and a reduction in body weight.^{R-3} With the dose of 100 mg/kg, ulcers in the stomach and erosions or ulcerations in the small intestine were observed in every dog.^{R-1; 3}

Client Consultation

A sheet entitled *DeramaxxTM Chewable Tablets: Information for Dog Owners* is provided by the United States manufacturer for clients administering oral deracoxib to their dogs.^{R-2}

In providing consultation, consider emphasizing the following selected information:

Keeping water readily available during the treatment period to avoid dehydration

Never exceeding the prescribed daily amount without veterinary consultation; contacting a veterinarian if more than the daily dose is consumed^{R-2}

Familiarizing clients with signs that an adverse reaction may be occurring, including vomiting, change in bowel movements, change in drinking habits, change in urination habits, or a decrease in appetite.^{R-2} Instructing them to discontinue medication and contact their veterinarian if a reaction is

suspected
Not administering nonsteroidal anti-inflammatory drugs labeled for human use to animals without guidance from a veterinarian; human dosages may be toxic or fatal for animals

Veterinary Dosing Information

Oral administration

Postprandial administration of deracoxib is recommended because bioavailability is highest when it is given with food; however, bioavailability is sufficient even if it must be given to a fasted dog.^{R-1;2}

For perioperative administration

Because nonsteroidal anti-inflammatory drugs (NSAIDs) can produce renal complications in animals prone to them, intravenous fluid therapy during surgery may be an appropriate precaution in some animals at risk for renal disease.^{R-1}

Oral Dosage Forms

DERACOXIB TABLETS

Usual dose:

Inflammation, musculoskeletal¹; or
Pain, musculoskeletal¹—*Dogs*: Oral, 1 to 2 mg per kg of body weight every twenty-four hours.^{R-1}
Inflammation, postoperative¹; or
Pain, postoperative¹—*Dogs*, at least 1.8 kg (4 pounds) of body weight: Oral, 3 to 4 mg per kg of body weight every twenty-four hours, for up to seven days.^{R-1}

Note: In clinical trials that demonstrated efficacy in treatment of postoperative pain and inflammation in dogs, deracoxib was administered the evening before surgery and then once a day for six days.^{R-1}

Product labeling states that deracoxib is effective when a dog has been fasted, although it is preferably administered with food.^{R-1}

Strength(s) usually available:

U.S.—^{R-1}
Veterinary-labeled product(s):
25 mg (Rx) [*Deramaxx* (chewable with flavoring; scored)].
100 mg (Rx) [*Deramaxx* (chewable with flavoring; scored)].
Canada—
Veterinary-labeled product(s):
Not commercially available.

Caution: Keep out of the reach of children.^{R-1}

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F),^{R-1} unless otherwise specified by manufacturer.

USP requirements: Not in USP.^{R-5}

¹Not included in Canadian product labeling or product not commercially available in Canada.

Developed: 2/6/04

References

1. Deramaxx Chewable Tablets package insert (Novartis—US), Rev 11/02, Rec 9/5/03.
2. Deramaxx chewable tablets: information for dog owners (Novartis—US), Rev 10/02. Available at www.deramaxx.com. Accessed August 29, 2003.
3. Deramaxx (deracoxib) chewable tablets freedom of information summary (NADA # 141-203 [perioperative]). Sponsor: Novartis Animal Health US. Approval Date: 8/21/02.

4. Deramaxx (deracoxib) chewable tablets freedom of information summary (Supplemental NADA # 141-203 [osteoarthritis]). Sponsor: Novartis Animal Health US. Approval Date: 2/11/03.
5. The United States pharmacopeia. The national formulary. USP 26th revision (January 1, 2003). NF 21st ed (January 1, 2003). Rockville, MD: The United States Pharmacopeial Convention, Inc., 2002.
6. Gierse JK, Staten NR, Casperson GF, et al. Cloning, expression, and selective inhibition of canine cyclooxygenase-1 and cyclooxygenase-2. *Vet Therapeutics* 2002; 3(3): 270-80.
7. Committee comment, Rec 10/22/03.