Mavacoxib

- (mav-ah-cox-ib)
- *Trocoxil®*
- Long-Acting NSAID

**Prescriber Highlights**

- Very long acting NSAID for dogs; half life averages 16-17 days. At time of writing (2014) not available in the USA.
- Limited clinical experience, but appears to be relatively safe and effective.
- Adverse effect profile expected to be similar to other canine-approved NSAIDs.
- Primary benefit appears to be for patients whose owners have difficulty adhering to a daily oral dosing regimen; but adverse effects may persist as well.

**Uses/Indications**

Mavacoxib is a very long acting oral NSAID that is licensed for use in dogs in the UK, Europe and elsewhere. In the UK it is labeled “for the treatment of pain and inflammation associated with degenerative joint disease in dogs aged 12 months or more in cases where continuous treatment exceeding one month is indicated.” At present, its place in the NSAID armamentarium for canine use is yet to be determined. It could be of benefit in those cases where owners have difficulty adhering to a daily oral dosing regimen, but because of its long half-life and duration of action, adverse effects could persist for many weeks after the drug was last given.

In a study comparing the safety and efficacy of mavacoxib with carprofen in 124 dogs, efficacy comparing the two were statistically equivalent and each had a similar rate and profile of adverse effects (Johnson et al. 2009).

**Pharmacology/Actions**

In dogs, mavacoxib appears to be a relative selective inhibiting cyclooxygenase (COX)-1 versus COX-2. It is believed to predominantly inhibit cyclooxygenase-2 (COX-2) and spare COX-1 at therapeutic dosages. This, theoretically, would inhibit production of the prostaglandins that contribute to pain and inflammation (COX-2) and spare those that maintain normal gastrointestinal and renal function (COX-1). However, COX-1 and COX-2 inhibition studies are done *in vitro* and do not necessarily correlate perfectly with clinical effects seen in actual patients.

**Pharmacokinetics**

Pharmacokinetic values for mavacoxib in dogs are widely patient variable. Average bioavailability after oral dosing is $\approx 46\%$ when fasted, but nearly doubles ($87\%$) when given with food. Peak levels occur in $\approx 11$ hours, but range widely. In most dogs, blood levels of those thought to be therapeutic occur in approximately one hour after dosing when given with food. Apparent volume
of distribution (steady-state) averaged 1.6 L/kg and the drug is highly bound to canine plasma proteins (98%). Total body clearance was a very low 2.7 mL/hour/kg and it is primarily cleared by biliary excretion. The average terminal half-life was 16.6 days (range: 8-39 days) (Cox, S. et al. 2010a). A population pharmacokinetic study by the same research group, reported a typical elimination half-life of 44 days, but ≈5% of patients had Bayesian estimates of >80 days (Cox, S.R. et al. 2011).

**CONTRAINDICATIONS/ PRECAUTIONS/ WARNINGS**

The UK labels lists the following contraindications: Dogs less than 12 months of age and/or less than 5 kg body weight, dogs with GI disorders including ulceration and bleeding, evidence of a hemorrhagic disorder, impaired renal or hepatic function, cardiac insufficiency, (history of) hypersensitivity to the active substance, sulfonamides or to any of the excipients. Do not use in pregnant, breeding or lactating animals or use concomitantly with glucocorticoids or other NSAIDs. Do not administer other NSAIDs within 1 month of the last administration of mavacoxib. It also states to avoid use in any dehydrated, hypovolemic or hypotensive animal, as there is a potential risk of increased renal toxicity. Concurrent administration of potentially nephrotoxic medicinal products should be avoided.

Animals should not become dehydrated when receiving this or other NSAIDs.

**ADVERSE EFFECTS**

As mavacoxib is a new agent, its adverse effect profile has not been fully determined in dogs; field studies have indicated that it causes similar adverse effects seen with other NSAIDs, but it is not known if this drug will have fewer or greater incidences of adverse effects when compared with other FDA-approved NSAIDs. NSAID adverse effects in dogs can include inappetence, diarrhea, vomiting, depression and renal toxicity.

**REPRODUCTIVE/ NURSING SAFETY**

The safety of mavacoxib has not been established during pregnancy and lactation. The UK label states: Do not use in pregnant, breeding or lactating animals. Studies in pregnant rabbits with another coxib-class NSAID (firocoxib) at dosages approximating those given to dogs, demonstrated maternotoxic and fetotoxic effects.

**OVERDOSAGE/ ACUTE TOXICITY**

In overdose safety studies performed in dogs, repeated doses (at labeled dosage frequency) of 5 and 10 mg/kg did not demonstrate adverse events, abnormal clinical chemistry or significant histological abnormalities. At 15 mg/kg, vomiting, softened/mucoid feces and increases in clinical chemistry parameters reflecting decreased renal function were noted. Doses of 25 mg/kg cause GI ulceration. One study dog died from GI perforation and peritonitis at the 25 mg/kg dose (Krautmann et al. 2009).
Oral acute overdoses of mavacoxib, should be managed as with other NSAID toxicity, but because of the drug’s very long duration of effect, prolonged monitoring and treatment may be required; consulting a veterinary poison center or the drug sponsor’s hotline seems prudent until more experience has been gained with this agent.

As with any NSAID, overdosage can lead to gastrointestinal and renal effects. The ASPCA Animal Poison Control Center (APCC) has not yet set a dosage level of concern for renal damage for dogs or cats. Decontamination with emetics and/or activated charcoal is appropriate. For doses where GI effects are expected, the use of gastrointestinal protectants is warranted. If renal effects are also expected, fluid diuresis is warranted.

**Drug Interactions**

At the time of writing, no drug interactions have been reported with mavacoxib, but the manufacturer warns that use in conjunction with other NSAIDs or corticosteroids be avoided. It is also possible mavacoxib could cause increased renal dysfunction if used with other drugs that can cause or contribute to renal dysfunction (e.g., diuretics, aminoglycosides), but the clinical significance of this potential interaction is unclear. The following drug interactions are either expected or are for dogs receiving mavacoxib and may be of clinical significance:

- **ACE inhibitors** (e.g., enalapril, benazepril): Some NSAIDs can reduce effects on blood pressure. Because ACE inhibitors potentially can reduce renal blood flow, use with NSAIDs could increase the risk for renal injury. However, one study in dogs receiving tepoxalin did not show any adverse effect. It is unknown what effects, if any, occur if other NSAIDs and ACE inhibitors are used together in dogs.

- **Aspirin**: May increase the risk of gastrointestinal toxicity (e.g., ulceration, bleeding, vomiting, diarrhea). Washout periods several weeks long are probably warranted when switching from mavacoxib to aspirin therapy in dogs.

- **Corticosteroids** (e.g., prednisone): May increase the risk of gastrointestinal toxicity (e.g., ulceration, bleeding, vomiting, diarrhea).

- **Digoxin**: NSAIDs may increase serum levels.

- **Fluconazole**: Administration has increased plasma levels of celecoxib in humans and potentially could also affect mavacoxib levels in dogs.

- **Furosemide**: NSAIDs may reduce saluretic and diuretic effects.

- **Methotrexate**: Serious toxicity has occurred when NSAIDs have been used concomitantly with methotrexate; use together with extreme caution.

- **Nephrotoxic Drugs** (e.g., furosemide, aminoglycosides, amphotericin B, etc.): May enhance the risk of nephrotoxicity development.

- **NSAIDS, Other**: May increase the risk of gastrointestinal toxicity (e.g., ulceration, bleeding, vomiting, diarrhea). The UK label states: “Should another NSAID be administered after
Trocoxil® treatment, a treatment-free period of at least ONE MONTH should be ensured to avoid adverse effects.” However, because of its very long half-life (up to 39 hours in one study dog) (Cox, S.R. et al. 2010b), mavacoxib may have a conservative washout time of 195 days (KuKanich et al. 2012).

LABORATORY CONSIDERATIONS

- None identified.

DOSES

Dogs:

- U.K. Label: For the treatment of pain and inflammation associated with degenerative joint disease in dogs aged 12 months or more in cases where continuous treatment exceeding one month is indicated (extra-label in USA): 2 mg/kg PO given immediately before or with the dog’s main meal. Care should be taken to ensure that the tablet is ingested. The treatment should be repeated 14 days later; thereafter the dosing interval is ONE MONTH. A treatment cycle should not exceed 7 consecutive doses (6.5 months). THIS IS NOT A DAILY NSAID. (Label Information—Trocoxil®; Pfizer U.K.)

MONITORING

- Baseline and periodic CBC and serum chemistry (including BUN/serum creatinine, and liver function assessment).
- Baseline history and physical.
- Efficacy of therapy.
- Adverse effect monitoring via client.

CLIENT INFORMATION

- Give doses exactly as directed by veterinarian, do not give extra doses or increase the dose without veterinarian’s guidance. This drug is NOT given every day. After the first 2 doses given 2 weeks apart, it is given once a month for up to 5 doses, then an extra month off the drug is needed if it is to be started again.
- Do not administer other NSAIDs within 1 month of the last dose of mavacoxib (e.g., carprofen, deracoxib, meloxicam, etc.).
- Give the medication with the dog’s largest meal of the day. The drug is much better absorbed from the stomach if given with food.
- Contact the veterinarian if any of the following adverse effects persist or are severe: loss of appetite, vomiting, change in bowel movements (e.g., stool color), change in behavior,
decrease in water consumption, or urination; these could potentially occur after many weeks after the last dose was given. Immediately report to the veterinarian if any of the following adverse effects occur: bloody stool/diarrhea, bloody vomiting, or allergic reaction (facial swelling face, hives, red, itchy skin).

- Do not allow dog to become dehydrated while receiving this drug.
- Since dogs may find the chewable tablets’ taste desirable, the drug should be stored out of reach of animals and children.

**CHEMISTRY/SYNONYMS**

Mavacoxib is structurally related to the human NSAID celecoxib and categorized as a diaryl substituted pyrazole. Mavacoxib’s solubility in water is relatively low (0.006 mg/mL).

Mavacoxib may also be known as mavacoxibum; PHA 739,521; or UNII-YFT7X7SR77. A common trade name is Trocoxil®.

**STORAGE/StABILITY**

Store in the original packaging at room temperature out of reach of pets and children.

**COMPATIBILITY/COMPOUNDING CONSIDERATIONS**

No specific information noted.

**DOSAGE FORMS/REGULATORY STATUS**

**Veterinary-Labeled Products:**

None in USA at time of writing. In the UK and Europe: Mavacoxib Oral Chewable Tablets: 6 mg, 20 mg, 30 mg, 75 mg, & 95 mg; Trocoxil®; (Rx)

**Human-Labeled Products:** None.

**REVIZIONS/REFERENCES**

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