

Metacam® (meloxicam)

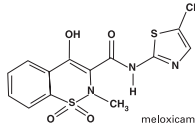
0.5 mg/mL Oral Suspension (equivalent to 0.02 mg per drop), 1.5 mg/mL Oral Suspension (equivalent to 0.05 mg per drop) and 5 mg/mL Solution for Injection.

Non-steroidal anti-inflammatory drug for oral or injectable use in dogs only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: Meloxicam is a Non-Steroidal Anti-Inflammatory (NSAID) drug of the oxamic class. Each milliliter of Metacam® Oral Suspension contains meloxicam equivalent to 0.5 milligrams or 1.5 milligrams and sodium benzoate (1.5 milligrams) as a preservative. Each mL of this sterile product for injection contains meloxicam 5.0 mg, alcohol 15%, glycolol 10%, poloxamer 188 5%, sodium chloride 0.6%, glycine 0.5% and meglumine 0.3%, in water for injection, pH adjusted with sodium hydroxide and hydrochloric acid.

The chemical name for Meloxicam is 4-Hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide. The suspension formulation is a yellowish viscous suspension with the odor of honey.



Clinical Pharmacology: Meloxicam has nearly 100% bioavailability when administered orally with food or after subcutaneous injection. The terminal elimination half life after a single dose is estimated to be approximately 24 hrs (+30%) regardless of route of administration. There is no evidence of statistically significant gender differences in drug pharmacokinetics. Drug bioavailability, volume of distribution, and total systemic clearance remain constant up to 5 times the recommended dose for use in dogs. However, there is some evidence of enhanced drug accumulation and terminal elimination half-life prolongation when dogs are dosed for 45 days or longer.

Peak drug concentrations can be expected to occur within about 2.5 and 7.5 hrs after subcutaneous and oral administration, respectively. Corresponding peak concentrations are approximately 0.734 and 0.464 mcg/mL following a 0.2 mg/kg subcutaneous and oral dose, respectively. Based upon intravenous administration in beagle dogs, the meloxicam volume of distribution in dogs (V_d) is approximately 0.32 Liters/kg (%CV = 21) and the total systemic clearance is 0.10 Liters/hr/kg (%CV = 13.1). The drug is 97% bound to canine plasma proteins.

Indications: Metacam® Oral Suspension and Metacam® 5 mg/mL Solution for Injection are indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Dosage and Administration: Always provide client information sheet with prescription. Carefully consider the potential benefits and risk of Metacam and other treatment options before deciding to use Metacam. Use the lowest effective dose for the shortest duration consistent with individual response. Metacam® Oral Suspension or Metacam® 5 mg/mL Solution for Injection (intravenously or subcutaneously) should be administered initially at 0.09 mg/lb (0.2 mg/kg) body weight only on the first day of treatment. For all treatments after day 1, Metacam® Oral Suspension should be administered once daily at a dose of 0.045 mg/lb (0.1 mg/kg).

Directions for Administration (Metacam® Oral Suspension):

Dogs under 10 pounds (4.5 kg)

Shake well before use, then remove cap. Particular care should be given with regard to the accuracy of dosing. **To prevent accidental overdosing of small dogs, administer drops on food only, never directly into the mouth.** Carefully measure suspension onto food to assure that the correct dose is given before presentation of the food to the dog. The syringe provided with Metacam® 0.5 mg/mL cannot be used to measure doses for dogs weighing less than 1 lb (0.45 kg) and the syringe provided with Metacam® 1.5 mg/mL cannot be used to measure doses for dogs weighing less than 5 lbs (2.3 kg).

Metacam® 0.5 mg/mL Oral Suspension

For dogs less than 1 lb (0.45 kg), Metacam® Oral Suspension can be given using the dropper bottle: two drops for each pound of body weight for the 0.5 mg/mL concentration (five drops for each kilogram of body weight), dropped directly onto the food.

For dogs between 1-10 pounds, Metacam® Oral Suspension can be given by drops or by using the measuring syringe provided in the package (see dosing procedure below). The syringe fits on to the bottle and has a scale beginning at 1 lb, designed to deliver the daily maintenance dose (0.05 mg/lb or 0.1 mg/kg). When using the syringe, the dog's weight should be rounded down to the nearest 1 pound increment. Replace and tighten cap after use.

Metacam® 1.5 mg/mL Oral Suspension

For dogs less than 5 lbs (2.3 kg), Metacam® Oral Suspension can be given using the dropper bottle: one drop for each pound of body weight for the 1.5 mg/mL concentration (two drops for each kilogram of body weight), dropped directly onto the food.

For dogs between 5-10 pounds, Metacam® Oral Suspension can be given by drops or by using the measuring syringe provided in the package (see dosing procedure below). The syringe fits on to the bottle and has a scale beginning at 5 lbs, designed to deliver the daily maintenance dose (0.05 mg/lb or 0.1 mg/kg). When using the syringe, the dog's weight should be rounded down to the nearest 5 pound increment. Replace and tighten cap after use.

Dogs over 10 pounds (4.5 kg)

Shake well before use then remove cap. Metacam® Oral Suspension may be either mixed with food or placed directly into the mouth. Particular care should be given with regard to the accuracy of dosing. Metacam® Oral Suspension can be given using the measuring syringe provided in the package (see dosing procedure below). The syringe fits on to the bottle and has a scale in pounds designed to deliver the daily maintenance dose (0.05 mg/lb or 0.1 mg/kg). When using the syringe, the dog's weight should be rounded down to the nearest 1 pound increment for Metacam® 0.5 mg/mL Oral Suspension and the nearest 5 pound increment for Metacam® 1.5 mg/mL Oral Suspension. Alternatively, Metacam® Oral Suspension can be given using the dropper bottle: two drops for each pound of body weight for the 0.5 mg/mL concentration (five drops for each kilogram of body weight) or one drop for each pound of body weight for the 1.5 mg/mL concentration (two drops for each kilogram of body weight). Replace and tighten cap after use.



Shake bottle well. Push down and unscrew bottle top. Attach the dosing syringe to the bottle by gently pushing the end onto the top of the bottle.



Turn the bottle/syringe upside down. Pull the plunger out until the black line on the plunger corresponds to the dog's body weight in pounds.



Turn the bottle right way up and with a twisting movement separate the dosing syringe from the bottle.



Push the plunger to empty the contents of the syringe.

Contraindications: Dogs with known hypersensitivity to meloxicam should not receive Metacam® Oral Suspension or Metacam® 5 mg/mL Solution for Injection. **Do not use Metacam® Oral Suspension in cats.**

Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion or injection by humans. **For oral or injectable use in dogs only.**

As with any NSAID all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to and periodically during administration of any NSAID. Owners should be advised to observe their dogs for signs of potential drug toxicity. Owners should be advised to observe their dogs for signs of potential drug toxicity and be given a client information sheet about Metacam.®

For technical assistance or to report suspected adverse reactions, call 1-866-METACAM (638-2226).

Precautions: The safe use of Metacam® Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating dogs has not been evaluated. Meloxicam is not recommended for use in dogs with bleeding disorders, as safety has not been established in dogs with these disorders.

Safety has not been established for intramuscular (IM) administration.

As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal and renal toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such antiprostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after administration of the total daily dose of Metacam Oral Suspension, a non-NSAID or non-corticosteroid class of analgesia should be considered. The use of another NSAID is not recommended. The use of concomitantly protein-bound drugs with Metacam® Oral Suspension or Metacam® 5 mg/mL Solution for Injection has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of Metacam® Oral Suspension or Metacam® 5 mg/mL Solution for Injection has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

Adverse Reactions: Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetence) were the most common adverse reactions associated with the administration of meloxicam. During two field studies, certain adverse reactions were observed. Of the dogs that took meloxicam (n=157), forty experienced vomiting, nineteen experienced diarrhea/soft stool, five experienced inappetence, and one each experienced bloody stool, bleeding gums after dental procedure, lethargy/swollen carpus, and epiphora. Of the dogs that took the placebo (n=149), twenty-three experienced vomiting, eleven experienced diarrhea/soft stool, and one experienced inappetence.

In foreign suspected adverse drug reaction (SADR) reporting over a 9 year period, incidences of adverse reactions related to meloxicam administration included: auto-immune hemolytic anemia (1 dog), thrombocytopenia (1 dog), polyarthritis (1 dog), nursing puppy lethargy (1 dog), and pyoderma (1 dog).

Information for Dog Owners: Meloxicam, like other NSAIDs, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with NSAID intolerance. Adverse reactions may include vomiting, diarrhea, lethargy, decreased appetite and behavior changes. Dog owners should contact their veterinarian immediately if possible adverse reactions are observed, and dog owners should be advised to discontinue Metacam therapy.

Post Approval Experience: The following adverse reactions are based on voluntary post-approval reporting. The categories are listed in decreasing order of frequency by body system.

Gastrointestinal: vomiting, anorexia, diarrhea, melena, gastrointestinal ulceration.

Urinary: Azotemia, elevated creatinine, renal failure.

Neurological/Behavioral/Special Sense: lethargy, depression.

Hepatic: elevated liver enzymes.

Dermatological/Immunological: Pruritus.

Effectiveness:

Metacam® (meloxicam) Oral Suspension: The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Both of the placebo-controlled, masked studies were conducted for 14 days. All dogs received 0.2 mg/kg on day 1. All dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14 of both studies. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement.

In the first field study (n=109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was demonstrated only for the overall investigator evaluation on day 7, and for the owner evaluation on day 14.

Metacam® (meloxicam) 5 mg/mL Solution for Injection: The effectiveness of meloxicam was demonstrated in a field study involving a total of 224 dogs representing various breeds, all diagnosed with osteoarthritis. This placebo controlled, masked study was conducted for 14 days. Dogs received a subcutaneous injection of 0.2 mg/kg meloxicam on day 1. The dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement. In this field study, dogs showed improvement with statistical significance after 14 days of meloxicam treatment for all parameters.

Palatability: Metacam® Oral Suspension was accepted by 100% of the dogs when veterinarians administered the initial dose into the mouth. Metacam® Oral Suspension was accepted by 90% of the dogs (123/136) when administered by owners. Problems associated with administration included refusal of food, resistance to swallowing and salivation.

Safety:

Six Week Study

In a six week target animal safety study, meloxicam was administered orally at 1, 3, and 5X the recommended dose with no significant clinical adverse reactions. Animals in all dose groups (control, 1, 3 and 5X the recommended dose) exhibited some gastrointestinal distress (diarrhea and vomiting). No treatment-related changes were observed in hematological, blood chemistry, urinalysis, clotting time, or buccal mucosal bleeding times.

Necropsy results included stomach mucosal petechiae in one control dog, two dogs at the 3X and one dog at the 5X dose. Other macroscopic changes included areas of congestion or depression of the mucosa of the jejunum or ileum in three dogs at the 1X dose and in two dogs at the 5X dose. Similar changes were also seen in two dogs in the control group. There were no macroscopic small intestinal lesions observed in dogs receiving the 3X dose. Renal enlargement was reported during the necropsy of two dogs receiving the 3X and two receiving the 5X dose.

Microscopic examination of the kidneys revealed minimal degeneration or slight necrosis at the tip of the papilla in three dogs at the 5X dose. Microscopic examination of the stomach showed inflammatory mucosal lesions, epithelial regenerative hyperplasia or atrophy, and submucosal gland inflammation in two dogs at the recommended dose, three dogs at the 3X and four dogs at the 5X dose. Small intestinal microscopic changes included minimal focal mucosal erosion affecting the villi, and were sometimes associated with mucosal congestion. These lesions were observed in the ileum of one control dog and in the jejunum of one dog at the recommended dose and two dogs at the 5X dose.

Six Month Study

In a six month target animal safety study, meloxicam was administered orally at 1, 3, and 5X the recommended dose with no significant clinical adverse reactions. All animals in all dose groups (controls, 1, 3, and 5X the recommended dose) exhibited some gastrointestinal distress (diarrhea and vomiting). Treatment-related changes seen in hematology and chemistry included decreased red blood cell counts in seven of 24 dogs (four 3X and three 5X dogs), decreased hematocrit in 18 of 24 dogs (including three control dogs), dose-related neutrophilia in one 1X, two 3X and three 5X dogs, evidence of regenerative anemia in two 3X and one 5X dog. Also noted were increased BUN in two 5X dogs and decreased albumin in one 5X dog.

Endoscopic changes consisted of reddening of the gastric mucosal surface covering less than 25% of the surface area. This was seen in three dogs at the recommended dose, three dogs at the 3X dose and two dogs at the 5X dose. Two control dogs exhibited reddening in conjunction with ulceration of the mucosa covering less than 25% of the surface area.

Gross gastrointestinal necropsy results observed included mild discoloration of the stomach or duodenum in one dog at the 3X and in one dog at the 5X dose. Multifocal pinpoint red foci were observed in the gastric fundic mucosa in one dog at the recommended dose, and in one dog at the 5X dose.

No macroscopic or microscopic renal changes were observed in any dogs receiving meloxicam in this six month study.

Microscopic gastrointestinal findings were limited to one dog at the recommended dose, and two dogs at the 3X dose. Mild inflammatory mucosal infiltrate was observed in the duodenum of one dog at the recommended dose. Mild congestion of the fundic mucosa and mild myositis of the outer mural musculature of the stomach were observed in two dogs receiving the 3X dose.

3 Day Target Animal Safety Study

In a three day safety study, meloxicam was administered intravenously to beagle dogs at 1, 3, and 5X the recommended dose (0.2, 0.6 and 1.0 mg/kg) for three consecutive days. Renal compromise with associated protein loss was the most significant clinical finding during the study. This occurred in the 5X group. Two dogs in the 5X group developed acute renal failure by the end of the study. Overall decreases in the means for total protein in the 3X and 5X groups were not clinically significant, ranging from 5.4 mg/dL and 5.5 mg/dL baseline, respectively, to 5.3 mg/dL for both groups at the study's end. Associated decreases in mean albumin values were seen in the 5X group, whose baseline mean of 2.9 mg/dL decreased to 2.5 mg/dL by Day 4.

Mean blood urea nitrogen (BUN) and creatinine values were increased only in the 5X group. The BUN increased from a baseline value of 14 mg/dL to 26 mg/dL by Day 4, while the creatinine increased from 0.9 mg/dL (baseline) to 1.1 mg/dL by Day 4. Increased mean urinary protein excretion was found to be both clinically and statistically significant in the 5X group, where mean values increased from 10 mg/dL (baseline) to 50 mg/dL by Day 4.

Vomiting occurred in one of six dogs in the 5X group. Fecal occult blood was also detected in three of six dogs in the 5X group.

Histologic examination revealed several renal changes, including dilated medullary and cortical tubules, interstitial inflammation, and renal papillary necrosis. This was seen in two of six dogs in both the 1X and 3X groups and in four of six dogs in the 5X group. Gastrointestinal lesions observed included superficial mucosal hemorrhages, congestion, and erosions. Mesenteric lymphadenopathy was identified in two of six dogs in the 1X group, four of six dogs in the 3X group, and five of six dogs in the 5X group.

Injection Site Tolerability

Meloxicam was administered once subcutaneously to beagle dogs at the recommended dose of 0.2 mg/kg and was well-tolerated by the dogs. Pain upon injection was observed in one of eight dogs treated with meloxicam. No pain or inflammation were observed post-injection. Long term use of Metacam® 5 mg/mL Solution for Injection in dogs has not been evaluated.

Effect on Buccal Mucosal Bleeding Time (BMBT)

Meloxicam (0.2 mg/kg) and placebo (0.4 mL/kg) were administered as single intravenous injections to 8 female and 16 male beagle dogs. There was no statistically significant difference (p<0.05) in the average BMBT between the two groups.

How Supplied:

Metacam® 5 mg/mL Solution for Injection: 10 mL vial

Metacam® Oral Suspension 0.5 mg/mL: 15 mL dropper bottle with measuring syringe

Metacam® Oral Suspension 1.5 mg/mL: 10, 32 and 100 mL dropper bottles with measuring syringe

Storage: Store Metacam® Oral Suspension at controlled room temperature 59-86°F (15-30°C).

Store Metacam® 5 mg/mL Solution for Injection at controlled room temperature, 68-77°F (20-25°C).

Manufactured by: Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO 64506, U.S.A.

US Patent 6,184,220

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Metacam® 1.5 mg/mL Oral Suspension Code 601511, 601521, 601531

Metacam® 0.5 mg/mL Oral Suspension Code 601411

Metacam® 5 mg/mL Solution for Injection Code 601311

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