## NADA 141-213, Approved by FDA **Metacam**®

## (meloxicam)

1.5 mg/mL Oral Suspension (equivalent to 0.05 mg per drop) 0.5 mg/mL Oral Suspension (equivalent to 0.02 mg per drop) Non-steroidal anti-inflammatory drug for oral use in dogs only

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

Warning: Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precaution for detailed information.

Description: Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class. Each milliliter of Metacam Oral Suspension contains meloxicam equivalent to 0.5 or 1.5 milligrams and sodium benzoate (1.5 milligrams) as a preservative. The chemical name for Meloxicam is 4-Hydroxy-Z-methyl-N-(S-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide-1, 1-dioxide. The formulation is a yellowish viscous suspension with the odor of honey. СН

Indications: Metacam Oral Suspension is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Osceparal 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 Cral Suspension 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). The syringe is calibrated to deliver the daily maintenance dose in pounds.

## Directions for Administration (1.5 mg/mL strength):

Directions for Administration (1.5 mg/mL strength): 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 the meloxicam concentration of 1.5 mg/mL cannot be used to measure doses for dogs weighing less than 5 los (2.3 kg).

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.

weight should be rounded down to the nearest 5 pound increment. Reprace and uginen cap area down. 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 5 pound increment. Alternatively, 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). Replace and tighten cap after use.

## Directions for Administration (0.5 mg/mL strength):

Directions for Auministration (0.5 mg/mL strengtur). 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 the meloxicam concentration of 0.5 mg/mL cannot be used to measure doses for dogs weighing less than 1 lb (0.45 kg).

For dogs less than 1 b (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 b, 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.

weight should be rounded down to the nearest 1 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/h) or 0.1 mg/kg). When using the syringe, the dog's weight should be rounded down to the nearest 1 pound increment. 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). Replace and tighten cap after use.



on to the top of the bottle.



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.

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Contraindications: Dogs with known hypersensitivity to meloxicam should not receive Metacam Oral Suspension. Do not use Metacam Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.

Do not use Metacam Oral Suspension in cats. Acuté renal failure and death have been associated with the use of meloxicam 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 by humans. For oral use in dogs only. As with any NASDL all dogs should undergo a thorough history and physical examination before the initiation of NSADD therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to and periodically during administration. Owner should be advised to observe their dog for signs of potential drug toxicity and be given a client information sheet about Metacam. Precautions: The safe use of Metacam Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lacitating dogs has not been established in dogs with these disorders. As a class, cyclo-oxygenase inhibitory NSADs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions from one NSAD may experience adverse reactions from another NSAD. Patients at greatest risk for renal toxicity are those that are delydrated, on concomitant diruterit therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSADD 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 on duce gastrointestinal autorations and/or perforations, concomitant that use with other anti-inflammatory drugs, such as NSAIDs or conficosteroid kass of form one NSAID or non-corticosteroid class of analgesia should be considered. The use of another NSAID or non-corticosteroid class of analgesia should be considered thouse of house



Adverse Reactions: Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetance) were the most common adverse reactions associated with the administration of meloxicam. The following table lists adverse reactions and the numbers of dogs that experienced them during the studies. Dogs may have experienced more than one episode of the adverse reaction during the study.

Characterized During Two Field Studi

Auverse Reactions Observed During two rield Statutes			
Clinical Observation	Meloxicam (n=157)	Placebo (n=149)	
Vomiting	40	23	
Diarrhea/Soft Stool	19	11	
Bloody Stool	1	0	
Inappetance	5	1	
Bleeding gums after dental procedure	1	0	
Lethargy/Swollen Carpus	1	0	
Epiphora	1	0	

In foreign suspected adverse drug reaction (SADR) reporting over a 9 year period, incidences of adverse reactions related to meloxicam administration included: auto-immung over a 9 year period, incidences of adverse reactions related to meloxicam administration included: auto-immung over a 9 year period, incidences of adverse reactions polyarhritis (1 dog), nursing puppy lethargy (1 dog), and pyoderma (1 dog).
Post-Approval Experience (Rev. 2010): The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse veractions are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of frequency by body system.
Gostrointestinal vormiting, anorexia, diarrhee, melena, gastrointestinal ulceration
Urinoary azotemia, elevated creatinine, renal failure
Neurological/Behavioral: lethargy, depression
Hepatic: levated liver enzymes

Hepatic: elevated liver enzymes

Hepatic: elevated liver enzymes Dermatologic: prurius Death has been reported as an outcome of the adverse events listed above. Acute renal failure and death have been associated with use of meloxicam in cats. To report suspected adverse drug events, for technical assistance, or to obtain a copy of the MSDS, contact Boehringer Ingelheim Vetmedica, Inc. at 1-866-METACAM (1-866-638-2260). For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.ida.gov/AnimalVeterinary/SafetyHealth.

Information for Dog Owners: Metacam, like other drugs of its class, 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 drug Should be advised of the potential for adverse reactions and be informed of the clinical signa associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue Metacam and contact their veterinarian immediately if signs of intolerance are observed. The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized, the drug is withdrawn, and veterinary care, if appropriate, is initiated. Owners should be advised to the importance of periodic follow up for all dogs during administration of any NSAID. Clinical Pharmacology: Medoxicam has nearly 100% bioavailability when administered orally with food. 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 genarce 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 7.5 hrs after oral administration to carine plasma proteins.

plasma proteins

plasma proteins. Effectiveness: 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 meloxicam 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 mprovement the first field study (n=109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters; however, statistical significance was demonstrated only for the overall investigator evaluation on day 7, and for the owners evaluation on day 1.4. Palatability: Metacam Oral Suspension was accepted by 100% of the dogs when veterinarians administered the initial

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:

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 with no significant clinical adverse reactions. Animals in all dose groups (control, 1, 3 and 5X the recommended dose) exhibited some gastorinetsinal distress (diarthea 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 lisions observed in dogs receiving the 5X dose. Microscopic examination or like three ossis at the tip of the papilia 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 for udogs at the 5X dose. Small intestinal microscopic changes included minima 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 <u>5iz Month Study</u> In a six month target animal safety study, meloxicam was administered orally at 1, 3, and 5X the recommended dose with to significant clinical adverse reactions. All animals in all dose groups (controls, 1, 3, and 5X the recommended dose with to significant clinical adverse reactions. All animals in all dose groups (controls, 1, 3, and 5X the recommended dose

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 adbode decreased and vomiting). Treatment related changes seen in thematology and chemistry included decreased and vomiting). Treatment related changes seen in hematoing the 18 of 24 dogs (including 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. Also noted were increased BUN in two 5X dogs and decreased albumin in one 5X dog. Also noted were increased BUN in two 5X dogs. 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 on junction with ulceration of the mucosa covering less than 25% of the surface area. Gross gastrointestinal necropsy results observed included mild discoloration of the sufface area. Gross gastrointestinal necropsy results observed included mild discoloration of the sufface area. No macroscopic or microscopic renal changes were observed in any dogs receiving meloxicam in this six month study. Microscopic renal changes were observed in any dogs receiving meloxicam in this six month study. Microscopic and in dis observed in the duodenum of one dog at the 5X dose. Mild inflammatory mucosal infiltrate was observed in the duodenum of one dog at the store commended dose, and two dogs at the 5X dose. Mild inflammatory mucosal infiltrate was observed in the duodenum of one dog at the store dose and two dogs at the 5X dose. Mild inflammatory mucosal infiltrate was observed in the duodenum of one dog at the stor

in two dogs find information in the fundic mucosa and mild myositis of the outer mural musculature of the stomach were observed in two dogs receiving the 3X dose.

### How Supplied:

Metacam Oral Suspension 1.5 mg/mL: 10, 32, 100 and 180 mL dropper bottles with measuring syringe. Metacam Oral Suspension 0.5 mg/mL 15 mL and 30 mL dropper bottles with measuring syringe. Storage: Store at controlled room temperature, 68-77°F (20-25°C). Excursions permitted between 59° and 86°F (15° and 30°C). Brief exposure to temperatures up to 104°F (40°C) may be tolerated provided the mean kinetic temperature does not exceed 77°F (25°C); however, such exposure should be minimized.

## Manufactured for-

# Boehringer Ingelheim Vetmedica, Inc. St. Joseph, MO 64506 U.S.A. US Patent 6,184,220

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Shake bottle well. Push down and unscrew bottle top. Attach the dosing syringe to the bottle by gently pushing the end weight in pounds.