NADA 141-213, Approved by FDA

# Metacam®

(meloxicam)

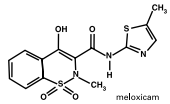
1.5 mg/mL Oral Suspension (equivalent to 0.05 mg per drop)
0.5 mg/mL Oral Suspension (equivalent to 0.02 mg per drop)

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




**Indications:** Metacam Oral Suspension is 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 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):**
**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 lbs (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.

**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):**
**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 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.

**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. 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.

*Shake bottle well. Push down and unscrew bottle top. Attach the dosing syringe to the bottle by gently pushing the end on to 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. **Do not use Metacam Oral Suspension in cats. Acute 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 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. 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 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. As a class, cyclo-oxygenase inhibitory NSAIDs 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 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 anti-prostaglandin 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. Consider appropriate washout times when switching from corticosteroid use or from one NSAID to another in dogs. The use of concomitantly protein-bound drugs with Metacam Oral Suspension 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 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 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.

**Adverse Reactions Observed During Two Field Studies**

| 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-immune hemolytic anemia (1 dog), thrombocytopenia (1 dog), polyarthritis (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 reactions 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.
*Gastrointestinal:* vomiting, anorexia, diarrhea, melena, gastrointestinal ulceration
*Urinary:* azotemia, elevated creatinine, renal failure
*Neurological/Behavioral:* lethargy, depression
*Hepatic:* elevated liver enzymes
*Dermatologic:* pruritus
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 (1-866-638-2226). For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.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 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 of the importance of periodic follow up for all dogs during administration of any NSAID.

**Clinical Pharmacology:** Meloxicam 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 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 7.5 hrs after oral administration. Corresponding peak concentration is approximately 0.464 mcg/mL following a 0.2 mg/kg oral dose. The drug is 97% bound to canine 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 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.

**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 dose 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.

**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

601413-03/6015268-03 601501-03
Revised 08/2014 08/2014

**Package Insert for Dogs**

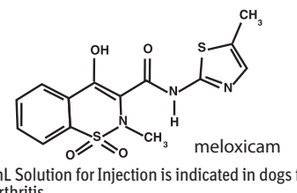
NADA 141-219, Approved by FDA

# Metacam®
(meloxicam)
**5 mg/mL Solution for Injection**
Non-steroidal anti-inflammatory drug for use in dogs and cats 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 Precautions for detailed information.**

**Description:** Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class. Each mL of this sterile product for injection contains meloxicam 5.0 mg, alcohol 15%, glycofurol 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.



meloxicam

**Indications:**
**Dogs:** Metacam (meloxicam) 5 mg/mL Solution for Injection is indicated in dogs for the control of pain and inflammation associated with osteoarthritis.

**Dosage and Administration:**
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.

**Dogs:** Metacam 5 mg/mL Solution for Injection should be administered initially as a single dose at 0.09 mg/lb (0.2 mg/kg) body weight intravenously (IV) or subcutaneously (SQ), followed, after 24 hours, by Metacam Oral Suspension at the daily dose of 0.045 mg/lb (0.1 mg/kg) body weight, either mixed with food or placed directly in the mouth.

**Contraindications:** Dogs with known hypersensitivity to meloxicam should not receive Metacam 5 mg/mL Solution for Injection.

**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 IV or SQ injectable use in dogs. All dogs should undergo a thorough history and physical examination before administering any NSAID. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to, and periodically during use of any NSAID in dogs.

**Owner should be advised to observe their dogs for signs of potential drug toxicity.**

**Precautions:**
The safe use of Metacam 5 mg/mL Solution for Injection in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating bitches 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 in dogs. When administering Metacam 5 mg/mL Solution for Injection, use a syringe of appropriate size to ensure precise dosing. As a class, cyclo-oxygenase inhibitory NSAIDs 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 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 anti-prostaglandin effects may result in clinically significant disease in patients with underlying or preexisting 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 the administration of the total daily dose of Metacam Oral Suspension, a non-NSAID or noncorticosteriod class of analgesia should be considered. The use of another NSAID is not recommended. Consider appropriate washout times when switching from corticosteroid use or from one NSAID to another in dogs. The use of concomitantly protein-bound drugs with 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 5 mg/mL Solution for Injection has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. The effect of cyclo-oxygenase inhibition and the potential for thromboembolic occurrence or a hypercoagulable state has not been studied.

**Adverse Reactions:**
**Dogs:** A field study involving 224 dogs was conducted. Based on the results of this study, 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 study. Dogs may have experienced more than one episode of the adverse reaction during the study.

| Adverse Reactions Observed During Field Study | | |
|---|---|---|
| **Clinical Observation** | **Meloxicam (n =109)** | **Placebo (n = 115)** |
| Vomiting | 31 | 15 |
| Diarrhea/Soft Stool | 15 | 11 |
| Inappetance | 3 | 0 |
| Bloody Stool | 1 | 0 |

In foreign suspected adverse drug reaction (SADR) reporting, 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).

**Post-Approval Experience (Rev. 2009):**
The following adverse reactions are based on post-approval adverse drug event reporting. The categories are listed in decreasing order of frequency by body system:
Gastrointestinal: *vomiting, diarrhea, melena, gastrointestinal ulceration*
Urinary: *azotemia, elevated creatinine, renal failure*
Neurological/Behavioral: *lethargy, depression*
Hepatic: *elevated liver enzymes*
Dermatologic: *pruritus*

Death has been reported as an outcome of the adverse events listed above. **Acute renal failure and death have been associated with the 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 (1-866-638-2226).

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

**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 behavioral changes. Dog owners should be advised when their pet has received a meloxicam injection. Dog owners should contact their veterinarian immediately if possible adverse reactions are observed, and dog owners should be advised to discontinue Metacam therapy.

**Clinical Pharmacology:** Meloxicam has nearly 100% bioavailability when administered orally or after subcutaneous injection in dogs. The terminal elimination half life after a single dose is estimated to be approximately 24 hrs (+/-30%) in dogs regardless of route of administration. 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 of 0.734 mcg/mL can be expected to occur within 2.5 hours following a 0.2 mg/kg subcutaneous injection in dogs. Based upon intravenous administration in Beagle dogs, the meloxicam volume of distribution in dogs (Vdλ) is approximately 0.32 L/kg and the total systemic clearance is 0.01 L/hr/kg. The drug is 97% bound to canine plasma proteins.

**Effectiveness:**
**Dogs:** The effectiveness of Metacam 5 mg/mL Solution for Injection 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 Metacam 5 mg/mL Solution for Injection on day 1. The dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14. Variables evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Variables assessed by owners included mobility, ability to rise, limping, and overall improvement.

In this field study, dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all variables.

**Animal Safety:**
**Dogs: 3 Day Target Animal Safety Study -** In a three day safety study, Metacam 5 mg/mL Solution for Injection was administered intravenously to Beagle dogs at 1, 3, and 5 times the recommended dose (0.2, 0.6 and 1.0 mg/kg) for three consecutive days. Vomiting occurred in 1 of 6 dogs in the 5X group. Fecal occult blood was detected in 3 of 6 dogs in the 5X group. No clinically significant hematologic changes were seen, but serum chemistry changes were observed. Serum alkaline phosphatase (ALP) was significantly increased in one 1X dog and two of the 5X dogs. One dog in the 5X group had a steadily increasing GGT over 4 days, although the values remained within the reference range. Decreases in total protein and albumin occurred in 2 of 6 dogs in the 3X group and 3 of 6 dogs in the 5X group. Increases in blood urea nitrogen (BUN) occurred in 3 of 6 dogs in the 1X group, 2 of 6 dogs in the 3X group and 2 of 6 dogs in the 5X group. Increased creatinine occurred in 2 dogs in the 5X group. Increased urine protein excretion was noted in 2 of 6 dogs in the control group, 2 of 6 dogs in the 1X group, 2 of 6 dogs in the 3X group, and 5 of 6 dogs in the 5X group. Two dogs in the 5X group developed acute renal failure by Day 4. Bicarbonate levels were at or above normal levels in 1 of the 3X dogs and 2 of the 5X dogs.

Histological examination revealed gastrointestinal lesions ranging from superficial mucosal hemorrhages and congestion to erosions. Mesenteric lymphadenopathy was identified in 2 of 6 dogs in the 1X group, 4 of 6 dogs in the 3X group, and 5 of 6 dogs in the 5X group. Renal changes ranged from dilated medullary and cortical tubules and inflammation of the interstitium, to necrosis of the tip of the papilla in 2 of 6 dogs in the 1X group, 2 of 6 dogs in the 3X group, and 4 of 6 dogs in the 5X group.

**Injection Site Tolerance -** Metacam 5 mg/mL Solution for Injection 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 was 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) -** Metacam 5 mg/mL Solution for Injection (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.

**Storage Information:** Store at controlled room temperature, 68-77°F (20-25°C). Use contents within 6 months of first puncture.

**How Supplied:**
Metacam 5 mg/mL Solution for Injection: 10 mL vial
NDC 0010-6013-01 - 10 mL

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

Metacam® is a registered trademark of Boehringer Ingelheim Vetmedica GmbH, licensed to Boehringer Ingelheim Vetmedica, Inc.

601307-07
Revised 08/2014
80724977, R.1

Boehringer Ingelheim

| Boehringer Ingelheim | |
|---|---|
| **Revision** | 2 |
| **Operator** | hal |
| **Date** | 06Aug14 |
| **Art #** | 601307-07 |
| **Item #** | 80724977 |
| **SAP#** | |
| **Product** | Metacam |
| **Type/Size** | Insert |
| **Template #** | 687 |
| **Dimensions** | 10.9375"H x 10.96875"W |
| **Fold** | 1.25" x 1.25" |
| **PDF** | 06Aug14 hal |

BLACK

B9L0
80724977, R.1
Metacam®
(meloxicam)
5 mg/mL Solution for Injection

B9L0
80724977, R.1
Metacam®
(meloxicam)
**5 mg/mL Solution for Injection**

**Package Insert for Cats**

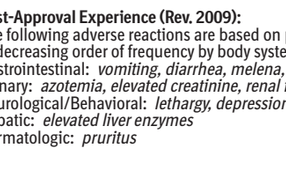
NADA 141-219, Approved by FDA

# Metacam®
(meloxicam)
**5 mg/mL Solution for Injection**
Non-steroidal anti-inflammatory drug for use in dogs and cats 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 Precautions for detailed information.**

**Description:** Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class. Each mL of this sterile product for injection contains meloxicam 5.0 mg, alcohol 15%, glycofurol 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.



meloxicam

**Indications:**
**Cats:** For the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration when administered prior to surgery.

**Dosage and Administration:**
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.

**Cats:** Administer **a single, one-time subcutaneous dose** of Metacam 5 mg/mL Solution for Injection to cats at a dose of 0.14 mg/lb (0.3 mg/kg) body weight. **Use of additional meloxicam or other NSAIDs is contraindicated. (See Contraindications).** To ensure accuracy of dosing, the use of a 1 mL graduated syringe is recommended.

**Contraindications:** Cats with known hypersensitivity to meloxicam should not receive Metacam 5 mg/mL Solution for Injection. Additional doses of meloxicam or other NSAIDs in cats are contraindicated, as no safe dosage for repeated NSAID administration has been established **(See Animal Safety). Do not use meloxicam in cats with pre-existing renal dysfunction.**

**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 subcutaneous (SQ) injectable use in cats. Do not use IV in cats.

**Do not administer a second dose of meloxicam.**
**Do not follow the single, one-time dose of meloxicam with any other NSAID.**
**Do not administer Metacam Oral Suspension following the single, one-time injectable dose of meloxicam.**

When administering any NSAID, appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to use in dogs and cats. All cats should undergo a thorough history and physical examination before administering meloxicam. **Do not repeat the single, one-time dose of meloxicam in cats.**

**Owner should be advised to observe their cats for signs of potential drug toxicity.**

**Precautions:**
The safe use of Metacam 5 mg/ml Solution for Injection in cats younger than 4 months of age, cats used for breeding, or in pregnant or lactating queens has not been evaluated.

Meloxicam is not recommended for use in cats with bleeding disorders, as safety has not been established in cats with these disorders. Safety has not been established for intravenous (IV) or intramuscular (IM) use in cats. When administering Metacam 5 mg/ml Solution for Injection, use a syringe of appropriate size to ensure precise dosing. As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Cats that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed.

**Patients at greatest risk for adverse events 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 and monitored. **Anesthetic drugs may affect renal perfusion; approach concomitant use of anesthetics and NSAIDs cautiously. Appropriate monitoring procedures should be employed during all surgical procedures. The use of perioperative parenteral fluids is recommended to decrease potential renal complications when using NSAIDs. If additional pain medication is needed after the single one-time dose of meloxicam, a non-NSAID class of analgesic may be necessary.**

In one study[1], one cat in each NSAID treatment group had increased intraoperative hemorrhage.

Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or gastrointestinal perforation, concomitant use of meloxicam with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided.

Consider appropriate washout times when switching from corticosteroid use to meloxicam in cats. **As a single use product in cats, meloxicam should not be followed by additional NSAIDs or corticosteroids.**

The use of concomitantly protein-bound drugs with Metacam 5 mg/ml Solution for Injection has not been studied in cats. Commonly used protein-bound drugs include cardiac, anticonvulsant, and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of Metacam 5 mg/ml Solution for Injection has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

The effect of cyclo-oxygenase inhibition and the potential for thromboembolic occurrence or a hypercoagulable state has not been studied.

**Adverse Reactions:**
**Cats:** A field study involving 138 cats was conducted. Of the 72 cats receiving Metacam 5 mg/mL Solution for Injection, six cats (8.3%) experienced post-treatment elevated serum blood urea nitrogen (BUN) levels. The pre-treatment values were in the normal range. Of the 66 cats in the butorphanol treatment group, no cats experienced post-treatment elevated serum blood urea nitrogen levels. Nine cats (12.5%) receiving Metacam 5 mg/mL Solution for Injection had post-treatment anemia. Pre-treatment, these cats all had hematocrit and hemoglobin values in the normal range. Four cats (6.1%) in the butorphanol treatment group had post-treatment anemia. All but one cat, who had a mild anemia pre-treatment (hematocrit=21% and hemoglobin=7.0 g/dL) had normal pre-treatment values. Twenty-four hours after the injection with Metacam 5 mg/mL Solution for Injection, one cat experienced pain upon palpation of the injection site.

**Foreign Experience:**
**Repeated use in cats has been associated with acute renal failure and death.** In studies used for the foreign approval of Metacam 5 mg/mL Solution for Injection in cats, lethargy, vomiting, inappetance, and transient pain immediately after injection were noted. Diarrhea and fecal occult blood have also been reported.

**Post-Approval Experience (Rev. 2009):**
The following adverse reactions are based on post-approval adverse drug event reporting. The categories are listed in decreasing order of frequency by body system:
Urinary: *azotemia, elevated creatinine, elevated phosphorus, renal failure*
Gastrointestinal: *anorexia, vomiting, diarrhea*
Neurologic/Behavioral: *lethargy, depression*
Hematologic: *anemia*

Death has been reported as an outcome of the adverse events listed above. **Acute renal failure and death have been associated with the 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 (1-866-638-2226).

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDAVETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

**Information For Cat 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 behavioral changes.

Cat owners should be advised when their pet has received a meloxicam injection. Cat owners should contact their veterinarian immediately if possible adverse reactions are observed.

**Clinical Pharmacology:** Meloxicam has nearly 100% bioavailability after subcutaneous injection in cats. The terminal elimination half life after a single dose is estimated to be approximately 15 hrs (+/-10%) in cats. Peak drug concentrations of 1.1 mcg/mL can be expected to occur within 1.5 hours following a 0.3 mg/kg subcutaneous injection in cats. The volume of distribution (Vdλ) in cats is approximately 0.27 L/kg, with an estimated total systemic clearance of 0.013 L/hr/kg. The drug is 97% bound to feline plasma proteins.

**Effectiveness:**
**Cats:** The effectiveness of Metacam 5 mg/mL Solution for Injection was demonstrated in a masked field study involving a total of 138 cats representing various breeds. This study used butorphanol as an active control. Cats received either a single subcutaneous injection of 0.3 mg/kg Metacam 5 mg/mL Solution for Injection or 0.4 mg/kg butorphanol prior to onychectomy, either alone or in conjunction with surgical neutering. All cats were premedicated with acepromazine, induced with propofol and maintained on isoflurane. Pain assessment variables evaluated by veterinarians included additional pain intervention therapy, gait/lameness score, analgesia score, sedation score, general impression score, recovery score, and visual analog scale score. Additionally, a cumulative pain score, which was the summation of the analgesia, sedation, heart rate and respiratory rate scores was evaluated. A palpometer was used to quantify the pain threshold.

A substantial number of cats required additional intervention in the 0-24 hour postsurgical period, with the majority of these interventions taking place within the first hour. Therefore, the percentage of cats in each group that received one or more interventions was designated as the primary assessment variable. Approximately half of the cats in each group received a pain intervention as a result of the first (time 0) post-surgical evaluation, i.e., extubation. At this point, the need to provide a pain intervention was not statistically significant between the two groups ($p=0.7215$). However, the median number of interventions was one per cat in the meloxicam group and two per cat in the butorphanol group and this difference was statistically significant ($p=0.0021$). The statistical evaluation supports the conclusion that the meloxicam test article is non-inferior to the butorphanol active control. Forty-eight of the 72 cats in the meloxicam group received one or more interventions (66.7%), and 47 of 66 cats in the butorphanol group received one or more interventions (71.2%). The number of interventions administered to the meloxicam group was less than the butorphanol group at 1, 3, 5, 8, 12, and 24 hours post-surgery.

Cats receiving Metacam 5 mg/mL Solution for Injection showed improvement in the pain assessment variables.

**Animal Safety:**
**Cats: 3 Day Target Animal Safety Study -** In a three day safety study, subcutaneous Metacam 5 mg/mL Solution for Injection administration to healthy cats at up to 1.5 mg/kg (5X the recommended dose) resulted in vomiting in three cats (1 of 6 control cats and 2 of 6 cats in 5X) and loose stools in four cats (2 of 6 control cats and 2 of 6 cats in 5X). Fecal occult blood was detected in ten of the twenty four cats, including two cats in the control group. This was not a dose-related event.

Clinically significant hematologic changes seen included increased PT and APTT in two cats (1 of 6 control cats and 1 of 6 cats in 5X), and elevated white blood cell counts in cats having renal or GI tract lesions. Serum chemistry changes observed included decreased total protein in four of 24 cats (1 of 6 cats in 1X, 2 of 6 cats in 3X and 1 of 6 cats in 5X), concomitant increases in blood urea nitrogen (BUN) and creatinine values in 2 of 6 cats in 5X.

Histological examination revealed gastrointestinal lesions ranging from inflammatory cell infiltration of the mucosa of the GI tract to erosions. Mesenteric lymphadenopathy was identified in 1 of 6 cats in 1X. Renal changes ranged from dilated medullary (2 of 6 cats in 1X, 1 of 6 cats in 3X, and 1 of 6 cats in 5X) and cortical (3 of 6 cats in 1X, 1 of 6 cats in 3X, and 3 of 6 cats in 5X) tubules and inflammation (2 of 6 cats in 1X, 2 of 6 cats in 3X, and 2 of 6 cats in 5X) or fibrosis (2 of 6 cats in 3X and 2 of 6 cats in 5X) of the interstitium to necrosis of the tip of the papilla (5 of 6 cats in 5X).

**Subsequent oral dosing -** In a nine day study with three treatment groups, Metacam 5 mg/mL Solution for Injection was given as a single subcutaneous injection using doses of 0 mg/kg (saline injection), 0.3 mg/kg and 0.6 mg/kg on Day 0. Metacam Oral Suspension, 1.5 mg/mL or saline was then administered orally once-daily at the same respective dose (0.3 or 0.6 mg/kg) for eight consecutive days. Clinical adverse reactions included vomiting, diarrhea, lethargy, and decreased food consumption in the treated groups, and one day of diarrhea in one control cat. The gross necropsy report includes observation of reddened GI mucosa in 3 of 4 cats in the 0.3 mg/kg group and 1 of 4 cats in the 0.6 mg/kg group. All saline-treated cats were normal. By Day 9, one cat in both the 0.3 mg/kg group and the 0.6 mg/kg group died and another cat in the 0.3 mg/kg group was moribund. The cause of death for these cats could not be determined, although the pathologist reported pyloric/duodenal ulceration in the cats in 0.6 mg/kg group. The safety studies demonstrate a narrow margin of safety.

**Injection Site Tolerance -** Histopathology of the injection sites revealed hemorrhage and inflammation, myofiber atrophy, panniculitis, fibrin deposition, and fibroblast proliferation. These findings were present in cats in all groups, with the 3X cats having the most present. No safe repeat dose has been established in cats.

**Storage Information:** Store at controlled room temperature, 68-77°F (20-25°C). Use contents within 6 months of first puncture.

**How Supplied:**
Metacam 5 mg/mL Solution for Injection: 10 mL vial
NDC 0010-6013-01 - 10 mL

**Reference:**
[1] Slingsby L.S., A.E. Waterman-Pearson. Comparison between meloxicam and carprofen for postoperative analgesia after feline ovariohysterectomy. Jour of Small Anim Pract (2002)43:286-289.

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

Metacam® is a registered trademark of Boehringer Ingelheim Vetmedica GmbH, licensed to Boehringer Ingelheim Vetmedica, Inc.

601307-07
Revised 08/2014
80724977, R.1