managing

Osteoarthritis

Think of the dog

you once knew…

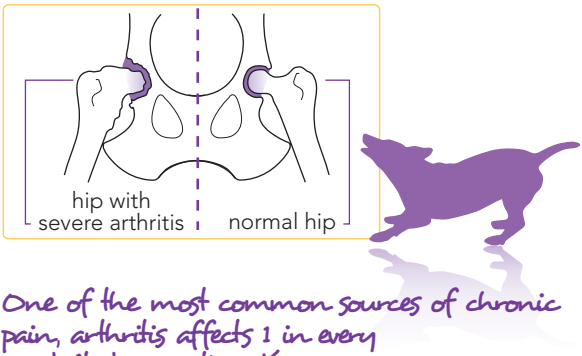
think

Spirited.

Healthy dogs love to run and jump and play

If you notice your dog is slowing down and is no longer as active as he used to be, you should discuss possible causes, including osteoarthritis, with your veterinarian.

Just like people, dogs can get arthritis. Also known as degenerative joint disease, osteoarthritis is a condition in which the joints become inflamed, swollen, and painful. Dogs with mild arthritis may have slight stiffness of the joints while those with more severe disease may have limping and lameness, but all arthritic dogs have some loss of mobility due to pain. The bones and joints most commonly affected are the hips, knees, elbows, shoulders, and spine.



One of the most common sources of chronic pain, arthritis affects 1 in every 5 adult dogs in the US.

(source: http://www.arthritis.org/resources/dogs/canine_arthritis_p1.asp)

How do dogs get arthritis?

Certain dogs are more likely to develop osteoarthritis than others. Some of the contributing factors are:

- Old age
- Large size
- Obesity
- Trauma or injury
- Genetic predisposition
- Inherited developmental abnormalities of the bones and joints
- Excessive physical activity

See accompanying Full Prescribing Information.

Does my dog have arthritis?

Sometimes it is hard to tell if dogs have arthritis. The signs may be subtle, and dogs can be good at hiding their pain. If you notice any of the following changes in your dog, talk to your veterinarian to discuss whether arthritis could be the cause:

- Difficulty climbing stairs, walking, running, or jumping
- Reluctance to play
- Lameness, limping, or moving with an altered gait
- Stiffness or slowness in rising from rest
- Soreness upon touching
- Frequent yelping or whimpering or lack of vocalization
- Excessive licking of a joint or leg
- Behavioral changes such as withdrawal or aggression
- Change in normal eating habits

It's not easy to see your pet in pain due to arthritis. However, it's important for you to recognize the signs and alert your veterinarian so arthritis can be diagnosed as soon as possible and proper treatment begun. Fortunately, early treatment of pain and inflammation can help control the progression of arthritis and allow your dog to remain comfortable longer.

Metacam®
(meloxicam)
Oral Suspension

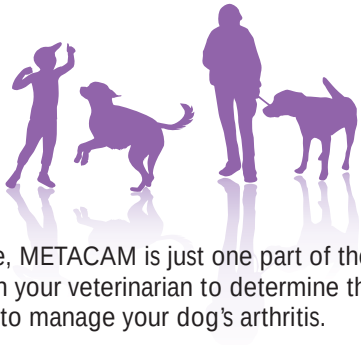
think

Playful.

How is arthritis treated?

Today, there are many treatments available to help dogs with arthritis. While it cannot be cured, *arthritis can be effectively managed* with pain-relieving medicines and supportive therapies.

Among the types of medications that have made arthritis treatment more promising in recent years are NSAIDs (nonsteroidal anti-inflammatory drugs). NSAIDs are used to control joint pain and inflammation to make it easier and less painful for dogs to move. Metacam® (meloxicam) is an NSAID that has enabled dogs worldwide to live more comfortable lives for over 15 years. A honey-flavored liquid, METACAM can be easily applied right on your dog's food or administered directly into your dog's mouth from the dispenser. One small dose of METACAM provides effective pain relief to help restore a dog's mobility all day long.



Of course, METACAM is just one part of the solution. Work with your veterinarian to determine the best program to manage your dog's arthritis.

Your management program may include:

- Controlling your dog's weight through diet and exercise
- Ensuring a comfortable living environment
- Performing physical therapy and massage
- Making daily activities easier and less painful
- Managing any other medical problems that exist

See accompanying Full Prescribing Information.

What can I expect from treatment?

When your dog starts METACAM treatment, you will likely notice that *your dog will be more energetic* and want to do more physically. It's important to remember that exercise should be increased slowly. Talk to your veterinarian about how much activity is best for your dog.

Also keep in mind that, as with all medicines, side effects may occur. These are usually mild but may be serious. The most common side effects are vomiting and soft stool or diarrhea.

If you notice any of the following signs in your dog during treatment, stop the drug and call your veterinarian:

- Vomiting or diarrhea
- Black, tarry-colored stools
- Eating less, change in drinking
- Change in urination habits (frequency, color, smell)
- Skin redness, scabs, or scratching
- Yellowing of the gums, skin, or whites of the eyes
- Lack of coordination
- Lethargy, depression, or aggression

Your veterinarian will determine the lowest effective dose of METACAM for your dog. It is important that you never give your dog more or less METACAM than your veterinarian prescribes.

Used properly, METACAM will help keep your dog pain-free and active and allow him to lead a more comfortable life.

Metacam®
(meloxicam)
Oral Suspension

think

Lively.

Your veterinarian may have started treatment in the clinic with Metacam® (meloxicam) Solution for Injection and recommended follow-up treatment at home with METACAM Oral Suspension.

Easy once-a-day dosing.

How long will a bottle of METACAM Oral Suspension last?

Oral Suspension 1.5 mg/mL					Oral Suspension 0.5 mg/mL	
	Bottle Size					Bottle Size
	180 mL	100 mL	32 mL	10 mL		15 mL
Body Weight (lbs)	Days of Treatment				Body Weight (lbs)	Days of Treatment
15	395	219	69	21	2.5	65
30	197	109	34	10	5	32
35	169	93	29	8	10	16
40	148	82	25	7	15	10
55	107	59	18	5	20	7
60	98	54	17	5	25	6
75	78	43	13	3	30	5
100	58	32	10	2		

For Large Dogs: Use the syringe supplied with the 1.5 mg/mL METACAM bottle. Draw up the prescribed amount of METACAM into the syringe based on your dog's weight and dispense either onto your dog's food or directly into his or her mouth. For dogs under 10 pounds, never administer drops directly into the mouth, only onto food.

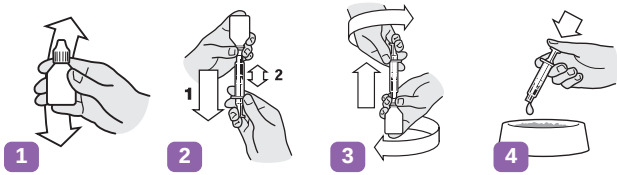
For Small Dogs: Use the syringe supplied with the 0.5 mg/mL concentration of METACAM designed specifically for small dogs. Draw up the prescribed amount of METACAM into the syringe based on your dog's weight and dispense either onto your dog's food or directly into his or her mouth. For dogs under 1 pound, never administer drops directly into the mouth, only onto food.

Shake well before administering medication.

See accompanying Full Prescribing Information.

METACAM Oral Suspension is easy to use.

- Calibrated syringe makes measuring the dose easy
- No multiple pill strengths or pill splitting
- Dogs love the honey flavor



1 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.

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

3 Turn the bottle right way up and with a twisting movement separate the dosing syringe from the bottle. Follow your veterinarian's instructions closely regarding how many drops to give and how they should be administered, since this can vary with the concentration of METACAM used and the weight of the dog. This is especially important for dogs weighing less than 10 pounds.

4 Push the plunger to empty the contents of the syringe. For dogs under 10 pounds, administer only on the food. If using the 0.5 mg/mL concentration, administer only on the food for dogs under 1 pound.

Metacam®
(meloxicam)
Oral Suspension

think

Fun-loving.

Frequently asked questions about Metacam® (meloxicam).

1 How long should my dog take METACAM?

Your veterinarian will recommend a treatment plan and may suggest that your dog try METACAM for a specific period of time. Your veterinarian may ask you to report back or return with your dog for an evaluation to determine if treatment should continue. Just like people who have arthritis, your dog will likely have to live with this condition for the rest of his life. You can feel comfortable giving METACAM knowing that it has been safely used to treat dogs with arthritis for over 15 years.

2 How does METACAM work?

METACAM targets and relieves both the pain and inflammation caused by osteoarthritis. Relief from arthritis pain can help restore mobility, allowing your dog to return to many of the activities that you both previously enjoyed.

3 What more can I do to help manage my dog's pain?

METACAM therapy is one of a number of things that may help relieve your dog's arthritis pain. Your veterinarian may suggest a weight loss program or exercise regimen. Talk to your veterinarian before starting your dog on any weight loss or exercise plan. You can also help to make your dog as comfortable as possible by providing a soft place to sleep and keeping him warm. Performing massage and physical therapy on your dog as directed by your veterinarian can relieve joint stiffness and increase range of motion.

See accompanying Full Prescribing Information.

4 Why can't I just give my dog aspirin?

Aspirin is a drug that is not approved for use in animals. Aspirin should not be given during METACAM therapy. Also, METACAM should not be given with other anti-inflammatory drugs such as cortisone, Rimadyl® (carprofen), ibuprofen, EtoGesic® (etodolac), Zubrin® (tepoxalin), Previcox® (firocoxib), or Deramaxx® (deracoxib). Be sure to tell your veterinarian about any other medications your dog is taking before beginning treatment with METACAM.

5 Why does METACAM come in a liquid form rather than a pill or tablet?

METACAM Oral Suspension is made in a smooth liquid form so that pet owners can dispense it easily from the syringe. Because it's liquid, it is easy to adjust the dose in small increments using the calibrated syringe, with a precision unavailable from a rigid tablet. Just as many children's medicines come in liquid rather than pill form, liquid METACAM is designed to make it easier to administer to dogs than pills. It is easily applied to the dog's food or given directly into the dog's mouth. Moreover, liquid METACAM is readily absorbed by dogs. And, dogs love the sweet honey-flavored taste. METACAM, the only NSAID available as an oral suspension, offers a highly convenient treatment option to pet owners.

6 Can METACAM be used in very small dogs?

Even small-breed dogs get arthritis. That's why a special low-concentration METACAM Oral Suspension for small dogs was developed. The syringe is marked in 1-lb increments to make fine-tuning of the dose easy for tiny dogs.

Metacam®
(meloxicam)
Oral Suspension

To the rescue.

Metacam® (meloxicam) is the Official NSAID of the National Disaster Search Dog Foundation (NDSDF).

The NDSDF is the nation's leading provider of trained search and rescue canines. These unique dogs, partnered with firefighters and other first-responders, provide a powerful service to society. The job of these teams is to find people buried alive in the wreckage of natural disasters and terrorist attacks. Their value became particularly apparent to the general public during the events of September 11th and Hurricane Katrina.

It costs NDSDF $10,000 to recruit, train, and provide long-term care for each new dog. Boehringer Ingelheim has committed $750,000 in support of the NDSDF over recent years, and the company's relationship with the organization continues to grow.

Search and rescue dogs are so driven to work, they may be less likely than average dogs to show when they are experiencing osteoarthritis-related pain. But if osteoarthritis pain is diagnosed, METACAM will be there to support these hard-working heroes.

NATIONAL DISASTER SEARCH DOG FOUNDATION

Metacam®
(meloxicam)
Oral Suspension

think
of life the way it used to be and the wonders of renewed vitality.

think
hope and promise.

think
Metacam® (meloxicam).

Veterinarian's Care Instructions

_____

_____

_____

_____

_____

Return Appointment

_____

Think of the dog you once knew.
Think METACAM.

Metacam®
(meloxicam)
Oral Suspension

1.866.METACAM (1.866.638.2226)
www.metacam.us
www.bi-vetmedica.com

Boehringer Ingelheim

NADA 141-213, Approved by FDA

Metacam®

(meloxicam)

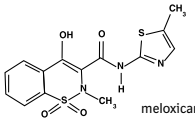
1.5 mg/mL Oral Suspension (equivalent to 0.05 mg per drop)
0.5 mg/mL Oral Suspension (equivalent to 0.02 mg per drop)

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.



meloxicam

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.

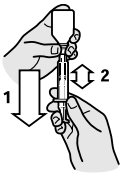
Directions for Administration (0.5 mg/mL strength):
Dogs under 10 pounds (4.5 kg)
Shake well before use, then remove cap. Particular care should be given with regard to the accuracy of dosing. **To prevent accidental overdosing of small dogs, administer drops on food only, never directly into the mouth.** 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 reactions, to obtain a Material Safety Data Sheet, or for technical assistance, call 1-866-METACAM (1-866-638-2226). For a complete listing of adverse reactions for meloxicam reported to the CVM see: http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055394.htm

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 dropper bottles with measuring syringe.
Storage: Store at controlled room temperature 59-86°F (15 - 30°C).

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

6015161L-06-1007/601401L-03-1007
Code 601511, 601521, 601531, 601571/601411
Revised 07/2010

601501-00
10/2010

601307L-05-1006

Package Insert for Dogs

NADA 141-219, Approved by FDA

Metacam®

(meloxicam)

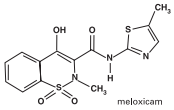
5 mg/mL Solution for Injection

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 reactions, to obtain a Material Safety Data Sheet, or for technical assistance, call 1-866-METACAM (1-866-638-2226).

For a complete listing of adverse reactions for meloxicam reported to the CVM see: *http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055394.htm*

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 SiteTolerance - 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).

How Supplied:

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

Manufactured for:

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

601307L-05-1006
Code 601311
Revised 06-2010