HUMAN-LABELED PRODUCTS:
Melatonin tablets are available in a variety of strengths from a variety of sources. Common strengths available range from 0.5 mg to 3 mg tablets. Sustained release capsules (3 mg) and oral liquid (500 mcg/mL) may also be available. Because melatonin is considered a "nutrient" there is no official labeling or central quality control systems for it in the USA. Purchase from reputable sources.

MELOXICAM

(mel-*ox*-i-kam) Metacam®

NONSTEROIDAL ANTIINFLAMMATORY AGENT

Prescriber Highlights

- NSAID used in dogs & cats; COX-2 preferential
- Available as both an injectable & oral product
- GI adverse effects can occur

Uses/Indications

Meloxicam is principally used for the symptomatic treatment of osteoarthritis in dogs. Short-term (single dose injectable) use is also approved (in the USA) for cats for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration when administered prior to surgery.

Pharmacology/Actions

Meloxicam has antiinflammatory, analgesic, and antipyretic activity similar to other NSAIDs. Like other NSAIDs, meloxicam exhibits analgesic, antiinflammatory, and antipyretic activity probably through its inhibition of cyclooxygenase, phospholipase A_2, and inhibition of prostaglandin synthesis. It is considered COX-2 preferential (not COX-2 specific) as at higher dosages its COX-2 specificity is diminished.

Acute dosing studies in dogs have not demonstrated any untoward renal or hepatic toxicity.

Pharmacokinetics

In dogs, meloxicam is well absorbed after oral administration. Food does not alter absorption. Peak blood levels occur in about 7–8 hours after administration. The volume of distribution in dogs is 0.3 L/kg and about 97% is bound to plasma proteins. Meloxicam is extensively biotransformed to several different metabolites in the liver; none of these appear to have pharmacologic activity. The majority of these (and unchanged drug) are eliminated in the feces. A significant amount of enterohepatic recirculation occurs. Elimination half-life is species specific. The elimination half-life in dogs averages 24 hours (range: 12–36 hours); other species: pigs: 4 hours; horses: 3 hours; cattle: 13 hours.

In cats, subcutaneous injection is nearly completely absorbed. Peak levels occur about 1.5 hours after injection. Meloxicam is relatively highly bound to feline plasma proteins (97%) and volume of distribution is about 0.27 L/kg. After a single dose, total systemic clearance is approximately 130 mL/hr/kg and elimination half life is approximately 15 hours.

Contraindications/Precautions/Warnings

Meloxicam is contraindicated in dogs hypersensitive to it. Safe use has not been evaluated in dogs less than 6 months old. The European label states that safe use has not been evaluated in dogs less than 6 weeks old. Although not part of the label, it should probably not be used in dogs with active GI ulceration or bleeding. It should be used with caution in patients with impaired hepatic, cardiac or renal function and hemorrhagic disorders.

Meloxicam is contraindicated in cats with known hypersensitivity to meloxicam or other NSAIDs. The manufacturer warns that additional doses of meloxicam or other NSAIDs are contraindicated as no safe dosage for repeated NSAID administration has been established. Use in cats less than 4 months of age has not been established. Use preoperatively for cats undergoing major surgery where hypotensive episodes are possible; may be at higher risk for renal damage.

The human label states that no dosage adjustment is necessary in patients with mild to moderate hepatic or renal impairment. Use extreme caution in dehydrated, hypovolemic, or hypotensive animals as there is a potential increased risk of renal toxicity developing.

Adverse Effects

Experience in Europe and Canada has demonstrated a relatively safe adverse effect profile for meloxicam in dogs. GI distress is the most commonly reported adverse effect, and in US field trials vomiting, soft stools, diarrhea, and inappetance were the most common adverse effects reported. Renal toxicity appears to be quite low. Postapproval adverse effects reported have included GI effects (vomiting, anorexia, diarrhea, melena, ulceration), elevated liver enzymes, pruritus, azotemia, elevated creatinine, and renal failure.

In cats, single doses of meloxicam appear relatively safe. In field trials some cats developed elevated BUN, post-treatment anemia and, rarely, residual pain at the injection site. In other studies, meloxicam has caused GI effects (vomiting, diarrhea, inappetance), behavior changes, and lethargy. Repeated use of meloxicam in cats had been associated with renal failure and death.

Reproductive/Nursing Safety

Safe use has not been established in dogs or cats used for breeding, or in pregnant or lactating animals. In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

Most NSAIDs are excreted in milk; use cautiously.

Overdosage/Acute Toxicity

The manufacturer warns to prevent accidental overdosing in small dogs, and to administer drops on food and not directly into the mouth. Treat symptomatically and supportively.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving meloxicam and may be of significance in veterinary patients:

- **ACE INHIBITORS** (*e.g.,* **enalapril, benazepril**): Some NSAIDs can reduce effects on blood pressure
- **ANTICOAGULANTS** (*e.g.*, **heparin**, **warfarin**, etc.): Increased chance for bleeding
- **ASPIRIN**: May increase the risk of gastrointestinal toxicity (*e.g.*, ulceration, bleeding, vomiting, diarrhea)
- **CORTICOSTEROIDS** (*e.g.,* **prednisone**): May increase the risk of gastrointestinal toxicity (*e.g.*, ulceration, bleeding, vomiting, diarrhea)
- **DIGOXIN**: NSAIDS may increase serum levels
- **FLUCONAZOLE**: Administration has increased plasma levels of celecoxib in humans and potentially could also affect meloxicam levels in dogs

- **FUROSEMIDE:** NSAIDs may reduce saluretic and diuretic effects
- **METHOTREXATE:** Serious toxicity has occurred when NSAIDs have been used concomitantly with methotrexate; use together with extreme caution
- **NEPHROTOXIC DRUGS** (*e.g.*, **furosemide**, **aminoglycosides**, **amphotericin B**, etc.): May enhance the risk of nephrotoxicity
- **NSAIDS, OTHER:** May increase the risk of gastrointestinal toxicity (*e.g.*, ulceration, bleeding, vomiting, diarrhea)

Doses

When doses are listed in "drops" use with caution, as drug concentration per drop may be different in products marketed in various countries.

- **DOGS:**

  For approved indications (osteoarthritis, analgesia, inflammatory conditions):

  a) Initially 0.2 mg/kg PO, IV or SC on the first day of treatment, subsequent doses of 0.1 mg/kg PO once daily in food or placed directly into mouth (not when dosing by the drop). (Package Insert; *Metacam® Injection/Oral Suspension*)

- **CATS:**

  For pain:

  a) For labeled indications: 0.3 mg/kg SC once (Label information; *Metacam® Injection for Cats*—BI)

  Note: The following dosages are extra-label in cats:

  b) 0.2 mg/kg PO initially, followed by 0.1 mg/kg PO (in food) once daily for 2 days and then 0.025 mg/kg 2–3 times a week (McLaughlin 2000)

  c) 0.1 mg/kg PO once daily (limit to 4 days use); 0.3 mg/kg IV or SC (one time use only) (Hardie 1997)

  d) For surgical pain: 0.2 mg/kg (or less) PO or SC once; 0.1 mg/kg (or less) SC, PO daily for 3–4 days

  For chronic pain: 0.2 mg/kg (or less) PO, SC once; 0.1 mg/kg (or less) PO for 3–4 days; 0.025 mg/kg PO (0.1 mg maximum dose per cat) 2–3 times weekly (Mathews 2000)

- **RABBITS, RODENTS:**

  For musculoskeletal and mild visceral pain:

  a) 0.2 mg/kg PO or SC once daily. Has a duration of action for 24–48 hours in most species; may be used for prolonged periods of time; also very effective when used in combination with opioids. (Mayer 2007)

Monitoring

- Clinical efficacy
- Adverse effects
- Renal function and hepatic function if used chronically

Client Information

- Shake oral liquid well before using.
- Carefully measure dose (oral liquid); do not confuse the markings on the syringe (provided by the manufacturer) with mL or kgs. If using drops to measure dose in small dogs, do not place drops directly into dog's mouth; mix with food. Otherwise, may place oral syringe into dogs mouth or mix with food.
- If animal develops adverse effects, contact the veterinarian
- If dispensed for outpatient use, obtain client information sheet for this medication

Chemistry/Synonyms

A COX-2 receptor preferential NSAID, meloxicam occurs as a pale yellow powder. It is in the oxicam class, related to piroxicam.

Meloxicam may also be known as: UH-AC-62, and UH-AC-62XX; many trade names are available.

Storage/Stability

Unless otherwise labeled, store the injection and oral liquid at room temperature.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Meloxicam Oral Suspension: 1.5 mg/mL (0.05 mg per drop in the USA product) in a honey-flavored base: 10 mL, 32 mL, 100 mL dropper bottles with measuring syringe (marked in 5 lb body weight increments); *Metacam®* (Boehringer Ingelheim Vetmedica); (Rx). Approved for use in dogs.

Meloxicam 5 mg/mL for Injection: 10 mL vial; *Metacam® Injection for Dogs* (Boehringer Ingelheim Vetmedica); (Rx). Approved for use in dogs.

Meloxicam 5 mg/mL for Injection: 10 mL vial; *Metacam® Injection for Cats* (Boehringer Ingelheim Vetmedica); (Rx). Approved for use in cats.

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Meloxicam Tablets: 7.5 mg & 15 mg; *Mobic®* (Boehringer Ingelheim/Abbott); generic; (Rx)

Meloxicam Oral Solution: 7.5 mg/5 mL in 100 mL; *Mobic®* (Boehringer Ingelheim/Abbott); Meloxicam (Roxane); (Rx)

In Canada, *Mobicox®* (Boehringer Ingelheim); (Rx)

MELPHALAN

(***mel***-fa-lan) **Alkeran®**

ANTINEOPLASTIC

Prescriber Highlights

- **Alkylating agent antineoplastic used for ovarian carcinoma, lymphoreticular neoplasms, osteosarcoma, mammary or pulmonary neoplasms, & multiple myeloma**
- **Contraindications (relative; risk vs. benefit): Anemia, bone marrow depression, current infection, impaired renal function, tumor cell infiltration of bone marrow, sensitivity to drug, or patients who have received previous chemotherapy or radiotherapy**
- **Adverse Effects: GI effects (anorexia, vomiting, diarrhea), pulmonary infiltrates or fibrosis, bone marrow depression (anemia, thrombocytopenia, leukopenia)**
- **Potential teratogen**
- **Determine dosages carefully**