Ketoprofen

Ketoprofen is a potent nonselective COX-1 inhibitor that has been used extensively in small animal medicine.

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Related terms:

Phenylbutazone, Meloxicam, Flunixin, Animals, Feeds, Dogs, Cats, Humans, Pain, Horses

Ketoprofen

Mark G. Papich DVM, MS, DACVCP, in Saunders Handbook of Veterinary Drugs (Fourth Edition), 2016

Indications and clinical uses

Ketoprofen is an NSAID and is used for treatment of moderate pain and inflammation. It has a half-life in most animals of less than 2 hours, but it has a duration of action for up to 24 hours. Ketoprofen is not approved in the United States for small animals, but has been labeled for dogs and cats in other countries. It has been given by injection for acute treatment and by tablet for long-term use. In dogs and cats, it has been shown effective for treating pyrexia. In horses, ketoprofen is used for musculoskeletal inflammation and pain, abdominal pain, and other inflammatory conditions. Ketoprofen also has been used in cattle, goats, sheep, and pigs. In cattle, it has been effective for fever, pain, and inflammation associated with mastitis. It is approved for use in cattle in Canada but not in the US.

Pain Assessment and Management

Turi K. Aarnes, William W. MuirIII, in Small Animal Pediatrics, 2011

Ketoprofen

Ketoprofen is a nonselective COX inhibitor in dogs and cats, although it is labeled for use only in horses. Available in both injectable and oral formulations, administration of ketoprofen in small animal practice has decreased as the result of the wide availability of COX-2 selective NSAIDs, which have fewer GI side effects. Ketoprofen is not recommended for use in young dogs and cats. When administered orally, ketoprofen should not be given with food because of decreased absorption (see Table 26-1). Ketoprofen is excreted by the kidneys unchanged and as a conjugated metabolite. Use of ketoprofen in the perioperative period has been associated with increased hemorrhage, in addition to the GI side effects associated with many NSAIDs.

Nonsteroidal Anti-inflammatory Drugs

Steven C. Budsberg, in Handbook of Veterinary Pain Management (Third Edition), 2015

Ketoprofen

Ketoprofen is a member of the arylpropionic acid class of NSAIDs. Ketoprofen inhibits both COX isoenzymes without selectivity in dogs. Because of this inhibition of both COX enzymes, ketoprofen is expected to have significant antithromboxane activity. Although ketoprofen can be used to effectively manage postoperative pain, there may be a propensity for postoperative hemorrhage. Ketoprofen is approved for use in dogs and cats in Europe and Canada in oral and parenteral formulations. The only data available to the clinician regarding clinical use of this product is in an acute pain model and perioperative pain management. Adverse events are the aforementioned excessive bleeding and GI

effects (primarily vomiting).

Nonsteroidal Antiinflammatory Drugs

Steven Budsberg, in Handbook of Veterinary Pain Management (Second Edition), 2009

Ketoprofen

Ketoprofen is a member of the arylpropionic acid class of NSAIDs.[75] Ketoprofen inhibits both COX isoenzymes without selectivity in dogs. Because of this inhibition of both COX enzymes, ketoprofen is expected to have significant antithromboxane activity.[14,29] Indeed, data show that although ketoprofen effectively manages postoperative pain, there is a propensity for hemorrhage perioperatively following the administration of ketoprofen.[40] Ketoprofen is approved for use in dogs and cats in Europe and Canada in oral and parenteral formulations. The only data available to the clinician regarding clinical use of this product are in an acute pain model and perioperative pain management.[29,40,76,77] Adverse events are the aforementioned excessive bleeding and GI effects (primarily vomiting).

Nonsteroidal anti-inflammatory drugs and chondroprotective agents

Peter D Hanson, Jill E Maddison, in Small Animal Clinical Pharmacology (Second Edition), 2008

Ketoprofen

(Ketofen®, Romefen®)

Clinical applications

Ketoprofen is registered for management of acute mild-to-moderate pain and at a lower dosage for osteoarthritis. It can be used in both dogs and cats. Several studies indicate that, except perhaps in the first postoperative hour, ketoprofen provides more effective, longer-lasting analgesia after soft tissue and orthopedic surgery than the synthetic opioids such as pethidine (meperidine), oxymorphone, buprenorphine and butorphanol.

Ketoprofen has been demonstrated to be an effective antipyretic agent in cats.

Formulations and dose rates

Ketoprofen is available in oral and injectable formulations.

DOGS

- 1 mg/kg IV, SC, IM or PO q.24 h for up to 5 d for acute pain and inflammation
- 0.25 mg/kg PO q.24 h for chronic pain, such as with osteoarthritis

CATS

- 1 mg/kg SC or PO q.24 h for 3–5 d

Mechanism of action – additional information

Ketoprofen is a member of the propionic acid class of NSAIDs. Depending on the species, tissue and assay system used, ketoprofen may inhibit lipoxygenase as well as COX. For example, it inhibits lipoxygenase in human lung tissue and rabbit leukocytes but not in guinea-pig lung. However, lipoxygenase inhibition by ketoprofen has not been demonstrated in vivo to date in domestic animals.

Ketoprofen is well absorbed orally but the presence of food or milk decreases oral absorption. The elimination half-life in cats and dogs is 3–5 h.

Adverse effects

- Ketoprofen appears to have a relatively good safety profile, although it is principally used for short courses only.
- The most common adverse effect is vomiting.
- Endoscopic studies suggest that ketoprofen is less ulcerogenic than aspirin but may be more likely to cause ulceration than carprofen.

Pharmacologic Principles

Jennifer L. Davis, in Equine Internal Medicine (Fourth Edition), 2018

Ketoprofen

Ketoprofen is a chiral propionic acid derivative approved for horses as a racemic solution for IV or IM injection. The label dose is 2.2 mg/kg administered once daily. Oral and rectal bioavailability is too poor for these routes to be used clinically.[367,457,458] Ketoprofen is 92.8% protein bound in horses.[459] Ketoprofen has a moderate Vd for both enantiomers of approximately 0.5 L/kg and short plasma elimination half-lives of 1 to 1.5 hours.[367,387,451,459,460] Ketoprofen is hepatically metabolized by conjugation reactions, with only 25% of a dose eliminated as unchanged drug in urine.[459] The S enantiomer is associated with antiprostaglandin activity and toxicity, whereas the R enantiomer is associated with analgesia and does not produce GI ulceration.[367,461] Because of chiral inversion, the S enantiomer predominates in horses.[367] Ketoprofen accumulates in inflammatory exudates in the horse, where the elimination half-life of the S enantiomer is 23 hours and the R enantiomer is 20 hours. The maximum antiinflammatory effects of ketoprofen occur at 4 hours after a dose and last for 24 hours, illustrating that the antiinflammatory effects are not related to plasma concentrations.[451] Similar to flunixin, ketoprofen pharmacokinetics are different in neonatal foals, and higher doses with longer dosing intervals are recommended.[462] In studies of noninfectious arthritis, endotoxemia, and colic, ketoprofen is clinically similar to flunixin meglumine in efficacy.[451,452,461] In an experimentally induced synovitis model, phenylbutazone was more effective in reducing lameness and synovial fluid prostaglandin concentrations.[463] In horses with chronic laminitis, ketoprofen was more effective than phenylbutazone at relieving pain but only at a higher-than-label dose (3.63 mg/kg).[464] In comparative toxicity studies in both horses and donkeys, ketoprofen at the label dose had less potential for toxicity than flunixin meglumine or phenylbutazone.[406,465] In drug tolerance studies using 25 times the label dose for 5 days, horses developed depression, icterus, nephritis, hepatitis, and hemorrhagic necrosis of the adrenal glands.[466]

Pharmacology of Analgesics

James E. Heavner, Dale M. Cooper, in Anesthesia and Analgesia in Laboratory Animals (Second Edition), 2008

1. Pharmacology

Ketoprofen and ibuprofen inhibit both COX-1 and COX-2, with ketoprofen having a higher selectivity for COX-1 than ibuprofen in dogs (Streppa et al., 2002). Carprofen is claimed to be predominately a COX-2-selective drug, but it does inhibit COX-1 slightly. Carprofen demonstrates less COX-2 selectivity in cats than in dogs (Clark, 2006; Streppa et al., 2002). Carprofen may also directly stimulate glycosoaminoglycan synthesis by chondrocytes (Benton et al., 1997). Metabolites of ketoprofen have also been shown to have activity against COX-1 and COX-2, and the selectivity of the metabolites is higher for COX-2 than the parent drug (Levoin et al., 2004). There may be activity that is not mediated by COX inhibition. The R-enantiomer of ketoprofen does not have any COX inhibitory activity, but has been shown to have antinociceptive activity in humans (Cooper et al., 1998). Some analgesic effects of ketoprofen may be mediated by serotonergic and noradrenergic mechanisms at the supraspinal and spinal levels (Diaz-Reval et al., 2004; Pinardi et al., 2001).

Avian Analgesia

Avian Analgesia

Joanne Paul-Murphy, Michelle G. Hawkins, in Fowler's Zoo and Wild Animal Medicine, 2012

Ketoprofen

Ketoprofen is a potent nonselective COX-1 inhibitor that has been used extensively in small animal medicine. The excellent oral bioavailability of ketoprofen in mammals makes this drug attractive for oral dosing. However, ketoprofen is most commonly used parenterally in birds because of limited oral PK data and difficulty in accurately dosing the oral formulation in small species. PK studies evaluating a single dose of 2 mg/kg ketoprofen given PO, IM, and IV in Japanese quail *(Coturnix japonica)* have shown very low oral (24%) and IM (54%) bioavailability of the drug and the shortest half-life reported for this NSAID in any species.[10] Additional studies are needed to determine whether drug formulations or physiologic differences between species could account for these differences. PD studies of 5 mg/kg IM ketoprofen in mallard ducks *(Anas platyrhynchos)* found an overall decrease in the inflammatory mediator TBX for approximately 12 hours after administration.[17] This suggests that the duration of anti-inflammatory effect in the mallards may parallel that of some mammals studied, and further studies are needed to evaluate the duration of effect and bioavailability in additional avian species. When ketoprofen (2 to 5 mg/kg IM) was administered to free-ranging spectacled eiders *(Somateria fischeri)* and king eiders *(Somateria spectabilis)*, four of ten male spectacled eiders and five of six male king eiders died within 1 to 4 days after surgery,[19] with histologic findings that included renal tubular necrosis, acute rhabdomyolysis, and mild visceral gout. Strong consideration was given to the male behaviors during mating season that may have predisposed these birds to dehydration and the adverse effects of COX inhibition.

Drug-induced ocular side effects

In Clinical Ocular Toxicology, 2008

Clinical significance

Ketoprofen rarely causes ocular problems. There has only been one case each of intracranial hypertension or a possible optic neuritis reported to the National Registry, so a causative relationship is highly unlikely. Ketoprofen, however, has been associated with precipitating cholinergic crises. It has also been associated with herpes simplex activation systemically and ocularly. We are not convinced that this agent causes keratoconjunctivitis sicca. However, since the drug is secreted in the tears, it would have the potential to aggravate patients with borderline sicca or those with pre-existing sicca. This agent is a photosensitizing agent may cause ocular phototoxicity. There is only one report (McDowell and McConnell 1985) of precipitating a cholinergic crisis in a patient with myasthenia gravis.

Nonsteroidal Antiinflammatories

Patricia A. Talcott MS, DVM, PhD, DABVT, Sharon M. Gwaltney-Brant DVM, PhD, DABVT, DABT, in Small Animal Toxicology (Third Edition), 2013

Ketoprofen

In dogs ketoprofen has been used for short-term anti inflammatory/analgesic use (up to 5 days).[2] Ketoprofen caused no adverse effects and was effective in cats at a dose of 2 mg/kg given subcutaneously, followed by 1 mg/kg PO every 24 hours for 4 days.[133] The antipyretic effect of ketoprofen in cats was rapid and persisted for at least 8 hours but less than 24 hours, and the authors reported no drug side effects based on clinical observation. The published dose for dogs is 2 mg/kg, followed by 1 mg/kg/day for 4 to 5 days.[38] Exposure doses of ketoprofen greater than 20 mg/kg may be associated with adverse effects. Management of ketoprofen overdoses is the same as for ibuprofen overdose: decontamination, gastrointestinal protection, and fluid diuresis, as indicated by degree of exposure.[114]

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