KETOPROFEN Veterinary—Systemic

Some commonly used *brand names* for veterinary-labeled products are: *Anafen* and *Ketofen*.

Some commonly used *brand names* for human-labeled products are: *Apo-Keto; Apo-Keto-E; Novo-Keto-EC; Orudis; Orudis-E; Orudis KT; Orudis-SR; Oruvail; Rhodis;* and *Rhodis-EC*.

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

Category: Analgesic; anti-inflammatory (nonsteroidal); antipyretic.

Indications

Note: Bracketed information in the *Indications* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

General considerations

Ketoprofen is a potent anti-inflammatory, with analgesic effects on par with carprofen or meloxicam.{R-67; 68; 70; 75}

Accepted

Inflammation, musculoskeletal (treatment); or
Pain, musculoskeletal (treatment)—

Horses: Ketoprofen injection is indicated in the control of inflammation and pain associated with musculoskeletal disorders.{R-2; 3; 8}

[*Cats*] and [*dogs*]: Ketoprofen is indicated in Canadian product labeling for the alleviation of inflammation and pain associated with musculoskeletal disorders.{R-4}

[*Cattle*]: Ketoprofen injection is indicated in Canadian product labeling for the alleviation of inflammation and pain associated with arthritis and traumatic musculoskeletal injuries.{R-3} See also the *Regulatory Considerations* section of this monograph.

[Fever (treatment)]—

Cats and *dogs:* Ketoprofen is indicated in Canadian product labeling for the symptomatic treatment of fever.{R-4; 29}

Cattle: Ketoprofen injection is indicated in Canadian product labeling for the symptomatic treatment of fever.{R-3} See also the *Regulatory Considerations* section.

[Inflammation (treatment)]; or
[Pain (treatment)]—*Cattle:* Ketoprofen injection is indicated in Canadian product labeling for the alleviation of inflammation and pain associated with a variety of nonmusculoskeletal conditions.{R-3} See also the *Regulatory Considerations* section.

[Mastitis, acute (treatment adjunct)]—*Cattle:* Ketoprofen is indicated in Canadian product labeling for the alleviation of fever, pain, and inflammation associated with acute clinical mastitis.{R-3; 31} It should be administered in conjunction with primary therapy, including antimicrobials, and supportive therapy.{R-31} One controlled, randomized study using repeated doses of ketoprofen showed significant improvement in outcomes for cows with acute clinical mastitis, including coliform mastitis.{R-31} See also the *Regulatory Considerations* section.

[Pain, postoperative (treatment)]—*Cats* and *dogs:* Ketoprofen is indicated in Canadian product labeling for the alleviation of postsurgical pain.{R-4} It can be effective when administered postoperatively, producing relief from pain that lasts for at least 12 to 24 hours.{R-63; 69-71}

Another nonsteroidal anti-inflammatory drug, carprofen, has been shown to have more efficacy in the control of postoperative pain if administered before rather than after surgery.{R-64} However, ketoprofen is considered a potent and relatively nonselective cyclooxygenase isozyme inhibitor, thereby having a greater potential than some nonsteroidal anti-inflammatory drugs for affecting renal and platelet function.{R-63; 68; 69; 71} General health and age of the

animal are considered in timing of administration (preoperative versus postoperative), anesthetic regimen, and use of intraoperative supportive therapy (see also *Veterinary Dosing Information* in this monograph). Preoperative ketoprofen administration would not be expected to significantly reduce the dose of thiopental required to induce anesthesia or the concentration of isoflurane required to maintain anesthesia in dogs.{R-63}

[Pain, visceral (treatment)][1]—*Horses:* Ketoprofen is used in the control of mild to moderate pain associated with colic.{R-26; 27} The underlying cause of colic should be determined and treated.

Acceptance not established

[Endotoxemia (treatment adjunct)]—*Calves:* There are insufficient data to establish the safety and efficacy of ketoprofen in the treatment of endotoxemia in calves; some toxic effects may be decreased or prevented, based on studies with experimentally induced disease.{R-14; 30} The treatment of endotoxemia should always include appropriate fluid and antimicrobial therapy. While the rapid rise in prostaglandin concentrations associated with endotoxemia is prevented by ketoprofen administration, hemodynamic changes do not always correlate with these concentrations and some animals may benefit much more than others.{R-14} See also the *Regulatory Considerations* section.

[Inflammation, general (treatment)][1]—*Goats* and *sheep:* There are insufficient data to establish the safety and efficacy of ketoprofen in the treatment of inflammatory conditions in goats and sheep; however, pharmacokinetic data available for lactating goats and sheep{R-47; 60; 61} are somewhat comparable to those for cattle. The administration of ketoprofen to the minor ruminant species might be considered, if clinically necessary. See also the *Regulatory Considerations* section.

[Pain, postoperative (treatment)][1]—*Calves:* There are insufficient data to establish the safety and efficacy of ketoprofen in the treatment of postoperative pain in calves; however, there is some evidence to suggest that it can be effective for certain procedures, such as castration or dehorning.{R-72-74}

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[1]Not included in Canadian product labeling or product not commercially available in Canada.

Regulatory Considerations

U.S.—

Ketoprofen is not labeled for use in food-producing animals in the U.S.{R-2} Under the Animal Medicinal Drug Use Clarification Act (AMDUCA) amendments to the Food, Drug, and Cosmetic Act, a nonsteroidal anti-inflammatory drug that is labeled for use in food-producing animals would be preferred over this product for use in those species.

The use of nonsteroidal anti-inflammatory drugs is restricted by specific guidelines set down by horse show organizations and racing commissions.{R-21}

Veterinary-labeled ketoprofen is available by prescription only.{R-2} Some products labeled for human use are available over-the-counter. See the *Dosage Forms* section.

Canada—

Ketoprofen is labeled for use in cattle but is not labeled for administration to horses to be slaughtered for use in food.{R-3; 4}

Veterinary-labeled ketoprofen is available by prescription only.{R-3; 4}

Chemistry

Chemical group: Propionic acid class of nonsteroidal anti-inflammatory agents.{R-17}

Chemical name: Benzeneacetic acid, 3-benzoyl-*alpha*-methyl-, (±)-.{R-1}

Molecular formula: $C_{16}H_{14}O_3$.{R-1}

Molecular weight: 254.28.{R-1}

Description: White or off-white, odorless, nonhygroscopic, fine to granular powder. Melts at about 95 °C.{R-45}

pKa: 5.02.{R-37}

Solubility: Freely soluble in ethanol, in chloroform, in acetone, and in ether; soluble in strong alkali; practically insoluble in water at 20 °C.[R-45]

Other characteristics: Highly lipophilic.[R-45]

Pharmacology/Pharmacokinetics

Note: See also *Table 1. Pharmacology/Pharmacokinetics,* at the end of this monograph.

Mechanism of action/Effect:

Anti-inflammatory—The mechanisms of action for the nonsteroidal anti-inflammatory drugs (NSAIDs) have not been completely illuminated.[R-1; 15] The primary mechanism of action for ketoprofen is considered to be inhibition of the cyclooxygenase pathway of arachidonic acid metabolism, leading to decreased production of prostaglandins.[R-2-4; 6; 15] Based on *in vitro* experiments, ketoprofen is considered one of the more potent inhibitors of prostaglandin synthesis.[R-51] It appears to be a relatively nonselective inhibitor of cyclooxygenase isozymes; ketoprofen inhibits COX-1 slightly more than COX-2 in some species and COX-2 slightly more than COX-1 in other species.[R-53; 61]

Normally, cell membrane damage triggers arachidonic acid metabolism and, by action of cyclooxygenase, production of short-lived endoperoxidases.[R-1; 15] The endoperoxidases are converted by other enzymes to thromboxane, prostaglandin E_2, prostaglandin $F_{2\alpha}$, prostacyclin, and oxygen radicals.[R-16] Inhibition of cyclooxygenase prevents the formation of these prostaglandins and the inflammation they cause.

However, certain nonsteroidal agents produce only minor antagonism of cyclooxygenase and still produce a significant anti-inflammatory effect.[R-6] It is not clear by what other pathways inflammatory mediators are blocked, although alteration of cellular and humoral immune responses and inhibition of other inflammatory mediators have been considered.[R-41] Arachidonic acid metabolism by the lipoxygenase pathway produces leukotrienes that are active in the inflammatory process and it is possible some NSAIDs inhibit lipoxygenase;[R-15] however, *in vivo* tests have not confirmed the inhibition of lipoxygenase by ketoprofen that was seen in some *in vitro* studies.[R-17; 19; 28; 38]

Antipyretic—Reduction of fever is believed to occur by inhibition of prostaglandins in the hypothalamus.[R-46]

Analgesic—The action of NSAIDs, such as ketoprofen, in the relief of pain is believed to be the interruption of mediators of inflammation, such as bradykinin, and prevention of their effect on peripheral pain endings.[R-93] NSAIDs also reduce the hyperalgesia that occurs in inflammation.[R-8; 15] Some evidence suggests that certain NSAIDs may produce some centrally induced analgesia, such as a spinal antinociceptive effect.[R-25]

Other actions/effects:

Antithrombosis—Ketoprofen is effective in inhibiting the production of thromboxane B_2,[R-19; 60; 61] a platelet aggregation promoter.

Gastrointestinal—The NSAIDS, such as ketoprofen, can cause gastrointestinal irritation that may lead to ulceration. Endogenous prostaglandins are believed to be part of the gastric defense system.[R-15] They inhibit gastric acid secretion and stimulate the production of protective mucus in the stomach and duodenum.[R-22] The decrease in prostaglandins caused by NSAIDs may decrease gastrointestinal cytoprotection, secretion of bicarbonate, and repair of tissue, eventually leading to vascular compromise in the gastrointestinal mucosa and subsequent tissue necrosis.[R-9; 10; 22; 23]

Renal—Prostaglandins produce or maintain vasodilation in the kidneys when necessary.[R-15] Animals with compromised hemodynamics become more vulnerable to ischemia and acute renal damage from the inhibition of prostaglandins.[R-15] Compromised animals chronically administered NSAIDs may be more susceptible to renal papillary necrosis.[R-15]

Chirality: Ketoprofen contains an asymmetrical carbon atom and exists in two enantiomeric forms. Differences in pharmacokinetics and pharmacodynamics between the two enantiomers occur in animals and can also vary significantly among species.{R-50} Currently, commercially available products contain a racemic (50:50) mixture of the two enantiomers, *S*(+) and *R*(–).

Conversion of *R*(–)-ketoprofen to *S*(+)-ketoprofen occurs in many species{R-50} but the extent varies from species to species, and in some circumstances, from animal to animal within a species. The percentage of total plasma ketoprofen identified as the *S*(+)-enantiomer 3 hours after administration of 20 mg of *R*(–)-ketoprofen per kg: gerbil (33%), mouse (44%), monkey (45%), guinea pig (47%), rabbit (51%), rat (74%), hamster (81%), dog (91.9%).{R-50} The chiral inversion of *R*(–)- to *S*(+)-ketoprofen after an intravenous dose of *R*-ketoprofen is reported to be 31% in calves, 37% in cats, 6 to 14% in sheep, 20% in horses with induced synovitis, and 49% in horses with only mild local inflammation.{R-33; 39; 54; 58; 60; 61} As the differing equine inversion percentages from two studies listed above suggest, conditions within an individual animal may change the extent of chiral inversion. This has also been demonstrated in a single study of dairy cattle, in which the percentage inversion was compared after an intravenous *R*(–)-enantiomer-dose of 0.5 mg/kg: preruminant calves (51%), cows in early lactation (33%), and cows in gestation (26%).{R-59}

The reverse process, conversion of *S*(+)-ketoprofen to *R*(–)-ketoprofen, has only been demonstrated in mice to date.{R-52}

Looking at inhibition of prostaglandin E_2 production in an *in vitro* cellular model as an assessment of activity, the *S*(+)-enantiomer was found to be 250 times more potent than the *R*(–)-enantiomer.{R-50} In an *in vivo* study of sheep with induced inflammation in tissue cages, *S*(+)-ketoprofen caused a much stronger inhibition for more than 4 times the duration of *R*(–)-ketoprofen.{R-60} Using a lipoxygenase assay, neither enantiomer had a significant effect.{R-50} Both enantiomers, administered separately, have a significant analgesic effect in mouse and rat models; some researchers believe *R*(–)-ketoprofen may produce analgesic effects but others suggest the effect seen is from *R*(–)-enantiomer converted to the *S*(+) or from *S*(+) contamination in *R*(–) isolates.{R-60}

The *S*(+)-enantiomer predominates in plasma, exudate and transudate, when the racemic mixture is administered intravenously to horses;{R-19} however, in sheep, *R*(–)-ketoprofen is found at a consistently higher concentration than *S*(–)-ketoprofen in plasma, exudate, and transudate.{R-60; 61}

Studies in dogs, horses, and sheep suggest that administration of the racemic mixture does not significantly affect the pharmacokinetics of each enantiomer.{R-51; 58; 60}

Absorption: Oral—

Cats and *dogs:* Veterinary-labeled tablets available in Canada are essentially completely absorbed and can be administered with or without food.{R-4}

Horses: An oil-based paste of micronized ketoprofen powder was not bioavailable to horses when administered orally; the same powder formulated in a hard gelatin capsule had an oral bioavailability of only about 52%.{R-57}

Protein binding: *Horses*—High (92%).{R-19; 55}

Biotransformation: Primarily hepatic, although excretion of metabolites into the urine also occurs.{R-41}

Onset of action:

Oral—*Cats* and *dogs:* 1 hour.{R-4}

Parenteral—*Horses:* Within 2 hours, with intramuscular or intravenous injection of 2.2 mg per kg of body weight (mg/kg).{R-2; 3}

Concentrations: Synovial fluid concentrations—*Horses:* Penetration of the *S*(+)-enantiomer into synovial fluid appears to be unaffected by

intravenous administration with the *R*(–)-enantiomer in a racemic mixture.[R-58]

Healthy horses—

Peak synovial ketoprofen concentration of 0.39 ± 0.03 microgram per mL (mcg/mL) at 1 hour after a 2.2 mg/kg intravenous dose of racemic ketoprofen.[R-35]

Stereospecific ketoprofen assays performed on synovial fluid after a 2.2 mg/kg intravenous dose of racemic ketoprofen:

R(–)-ketoprofen—0.47 ± 0.26 mcg/mL at 1 hour;[R-55] 0.40 ± 0.05 mcg/mL at 1 hour.[R-56]

S(+)-ketoprofen—0.58 ± 0.29 mcg/mL at 1 hour;[R-55] 0.41 ± 0.06 mcg/mL at 1 hour.[R-56]

Horses with synovitis—

Peak synovial ketoprofen concentration of 2.53 ± 0.39 mcg/mL at 1 hour after the 2.2 mg/kg intravenous dose.[R-35] At 3 hours after the dose, synovial fluid concentrations tend to be greater than plasma concentrations.[R-35]

Note: At 3 and 6 hours after the dose, synovial concentrations were not significantly different between healthy horses and horses with synovitis, but horses with synovitis also had more gradually declining concentrations, in this study requiring up to 9 hours to fall to 0.06 mcg/mL.[R-35]

In a study of stereospecific pharmacokinetics with induced synovitis, concentrations were no longer measurable after 4 to 6 hours. Peaks were:

R(–)-ketoprofen—0.32 ± 0.06 mcg/mL at 1 hour.[R-58]

S(+)-ketoprofen—0.49 ± 0.07 mcg/mL at 1 hour.[R-58]

Duration of action: There is no standardized method of measuring or predicting the duration of action of the NSAIDs. Serum concentrations may wane a considerable time before exudate or tissue concentrations and therefore are not predictive of duration of action at the treatment site.[R-18] For horses, the half-life of ketoprofen in plasma is about one twentieth that in induced exudates.[R-19]

Dogs: Postoperative analgesia, when administered preoperatively, is considered to be at least 12 to 20 hours.[R-67; 69]

Horses: Anti-inflammatory effect, as measured using an induced carpitis model, reaches a maximum at 12 hours and is still measurable at 24 hours when administered at a dose of 1.1 to 3.3 mg/kg.[R-2]

Elimination: *Cattle*—Eighty percent of a parenteral dose is eliminated in the urine within 24 hours of administration, primarily as conjugated metabolite.[R-3]

Precautions to Consider

Species sensitivity

Equids—Ketoprofen has not been evaluated in foals and ponies, which are susceptible to gastric ulceration from nonsteroidal anti-inflammatory drugs (NSAIDs).[R-3]

Pregnancy/Reproduction

The effect of ketoprofen on fertility, pregnancy, or fetal health has not been determined in most species.[R-2-4]

Cattle: A dose of 6 mg per kg of body weight (mg/kg), administered during the sixth week of gestation or administered between the second and ninth month of gestation, had no effect on measured parameters, such as fetal development, length of gestation, parturition, or calf viability.[R-3] Effects on the fertility of bulls has not been evaluated.[R-3]

Lactation

Cattle—Ketoprofen is distributed into milk in small amounts in some lactating cattle.[R-37] In healthy cattle administered an intravenous dose of 3.3 mg/kg, only a few milk samples collected up to 2 hours later contained a detectable amount of ketoprofen, between 27 and 90 nanograms per mL (nanograms/mL).[R-37]

Goats—Ketoprofen concentrations in milk were less than the 25 nanograms/mL limit of detection from eight to twenty-four hours

after intravenous administration of 2.2 mg/kg to six lactating goats.[R-47]

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Anti-inflammatory drugs, nonsteroidal
(concurrent use of more than one NSAID may greatly increase the risk of gastrointestinal ulceration and renal papillary necrosis)[R-5; 11]

Corticosteroids[R-22; 23]
(concurrent administration of corticosteroids with NSAIDs can exacerbate injury to the gastrointestinal tract caused by those medications)[R-22; 23]

Human drug interactions and/or related problems[R-49]

In addition to the above drug interactions reported in animals, the following drug interactions have been reported in humans, and are included in the human monograph *Anti-inflammatory Drugs, Nonsteroidal (Systemic)* in *USP DI Volume I;* these drug interactions are intended for informational purposes only and may or may not be applicable to the use of ketoprofen in the treatment of animals:

Note: All of the following interactions have not been documented with every NSAID. However, they have been reported with several and should be considered potential precautions to the use of any NSAID, especially with chronic administration.

Anticoagulants, coumarin- or indandione-derivative or
Heparin or
Thrombolytic agents
(inhibition of platelet aggregation by NSAIDs, and the possibility of NSAID-induced gastrointestinal ulceration or bleeding, may be hazardous to patients receiving anticoagulant or thrombolytic therapy)

Antidiabetic agents, oral or
Insulin
(NSAIDs may increase the hypoglycemic effect of these medications because prostaglandins are directly involved in regulatory mechanisms of glucose metabolism)

Antihypertensives, including angiotensin-converting enzyme (ACE) inhibitors, or
Diuretics
(NSAIDs may decrease the diuretic, natriuretic, and antihypertensive effects of diuretics, probably by inhibiting renal prostaglandin synthesis)
(concurrent use of an NSAID and a diuretic may increase the risk of renal failure secondary to a decrease in renal blood flow caused by inhibition of renal prostaglandin synthesis)

Aspirin or
NSAIDS, two or more concurrently
(concurrent use of two or more NSAIDS, including aspirin, is not recommended; concurrent therapy may increase the risk of gastrointestinal toxicity, including ulceration or hemorrhage, without providing additional symptomatic relief)
(concurrent administration of two or more NSAIDs may alter the pharmacokinetic profile of at least one of the medications, which may alter the therapeutic effect and/or increase the risk of adverse effects; specifically, aspirin decreases protein binding of ketoprofen and etodolac [but does not alter etodolac clearance], increases plasma clearance of ketoprofen, and interferes with the formation and excretion of ketoprofen conjugates)

Corticosteroids, glucocorticoid or
Corticotropin (chronic therapeutic use) or
Potassium supplements

(concurrent use with an NSAID may increase the risk of gastrointestinal side effects, including ulceration or hemorrhage; however, concurrent use with a glucocorticoid or corticotropin in the treatment of arthritis may provide additional therapeutic benefit and permit reduction of glucocorticoid or corticotropin dosage)

Cyclosporine or

Nephrotoxic medications, other

(inhibition of renal prostaglandin activity by NSAIDs may increase the plasma concentration of cyclosporine and/or the risk of cyclosporine-induced nephrotoxicity)

(the risk of adverse effects may also be increased when an NSAID is used concurrently with other nephrotoxic medications)

Digitalis glycosides

(diclofenac and ibuprofen have been shown to increase serum digoxin concentrations, and indomethacin has increased digitalis concentrations in neonates being treated for patent ductus arteriosus; the possibility should be considered that some of the other NSAIDs also may increase digoxin concentrations, leading to an increased risk of digitalis toxicity; increased monitoring and dosage adjustments of the digitalis glycoside may be necessary during and following concurrent NSAID therapy; however, studies have failed to show that flurbiprofen, ketoprofen, piroxicam, or tenoxicam increase digoxin concentrations, and phenylbutazone may decrease digitalis concentrations)

Methotrexate

(NSAIDs may alter the pharmacokinetics of methotrexate)

Platelet aggregation inhibitors, other

(concurrent use with an NSAID may increase the risk of bleeding because of additive inhibition of platelet aggregation, as well as the potential for NSAID-induced gastrointestinal ulceration or hemorrhage)

(concurrent use of sulfinpyrazone with NSAIDs may also increase the risk of gastrointestinal ulceration or hemorrhage)

Probenecid

(concurrent use of probenecid with ketoprofen is not recommended; probenecid decreases ketoprofen's renal clearance [by approximately 66%] and protein binding [by 28%], and inhibits formation and renal clearance of ketoprofen conjugates, leading to greatly increased ketoprofen plasma concentration and risk of toxicity)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Laboratory value alterations relating specifically to the use of ketoprofen in animals have been rarely reported in veterinary literature. Human laboratory value alterations have been reported and are included in the following section.

Human laboratory value alterations[R-49]

The following laboratory value alterations have been reported in humans, and are included in the human monograph *Anti-inflammatory Drugs, Nonsteroidal (Systemic)* in *USP DI Volume I;* these laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of ketoprofen in the treatment of animals:

With diagnostic test results

Albumin, urine, determinations and

Bile salts, urine, determinations and

17-Ketosteroid (17-KS), urine, determinations and

17-Hydroxycorticosteroid (17-OHCS), urine, determinations

(ketoprofen metabolites in urine may interfere with test procedures that rely on acid precipitation as an end point or on color reactions of carbonyl groups; no interference occurs in tests for urinary protein using commercially available dye-impregnated test strips)

With physiology/laboratory test values
Bleeding time
(may be prolonged by most NSAIDs [with ketoprofen, by 3 to 4 minutes above baseline values] because of suppressed platelet aggregation)
Hematocrit or
Hemoglobin
(values may be decreased, possibly because of gastrointestinal bleeding or microbleeding and/or hemodilution caused by fluid retention)
Leukocyte count and
Platelet count
(may be decreased)
Liver function tests, including:
Alkaline phosphatase and
Lactate dehydrogenase (LDH) and
Transaminases, serum
(values may be increased; liver function test abnormalities may return to normal despite continued use; however, if significant abnormalities occur, clinical signs and symptoms consistent with liver disease develop, or systemic manifestations such as eosinophilia or rash occur, the medication should be discontinued)
Potassium, serum
(concentrations may be increased)
Renal function tests, including:
Blood urea nitrogen (BUN)
Creatinine, serum
Electrolytes, blood and urine
Urine volume
(NSAIDs may decrease renal function, resulting in increased BUN, serum creatinine, and serum electrolyte concentrations and in decreased urine volume and urine electrolyte concentrations; however, in some cases, water retention may exceed that of sodium, resulting in dilutional hyponatremia)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

» Hypersensitivity to ketoprofen{R-3; 4}
(previous development of adverse effects from ketoprofen may be an indication of increased risk of future sensitivity)

» Gastrointestinal ulceration{R-4}
(many NSAIDs are known to increase the risk of gastrointestinal disease, particularly ulceration;{R-4} therefore, the presence of pretreatment lesions may put an animal at risk of exacerbation or perforation)

» Hepatic disease, severe{R-4}
(ketoprofen is metabolized by the liver)

» Renal disease, severe{R-4}
(because some NSAIDs are known to cause renal papillary necrosis in some circumstances,{R-11} risk to patients with renal compromise may be increased)

Risk-benefit should be considered when the following medical problem exists:

Coagulation disorders{R-4; 65; 67; 68}
(ketoprofen has antithrombotic effects; platelet aggregation is measurably decreased and under some circumstances, buccal mucosal bleeding time may be prolonged)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):

Hemoglobin determinations{R-1} and
Hematocrit determinations{R-1}

(may be indicative of chronic gastrointestinal blood loss)

Occult blood, fecal[R-1]

Stools, observe for black or tarry[R-19; 24]

(if black or tarry stools are observed, the cessation of therapy should be considered;[R-19] if stools are normal with long-term administration, to determine if chronic blood loss is occurring, positive fecal occult blood results in animals on a meatless diet should be followed by serum hemoglobin and hematocrit measurements;[R-1] fecal occult blood tests may be more sensitive than other noninvasive tests for detecting lower intestinal injury[R-23] but are unlikely to detect stomach blood loss[R-24])

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence more frequent

Cats and *dogs*

Vomiting (10.7% in cats; 4 to 6% in dogs in clinical efficacy studies)[R-4]

Incidence less frequent

Cats and *dogs*

Diarrhea (2.6% in cats; 2% in dogs in clinical efficacy studies)[R-4]

Incidence rare

Dogs

Anorexia (0.7%);[R-4] ***thirst, increased*** (0.7%)[R-4]

Human side/adverse effects[R-49]

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monograph *Anti-inflammatory Drugs, Nonsteroidal (Systemic)* in *USP DI Volume I;* these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of ketoprofen in the treatment of animals:

Incidence more frequent

Abdominal cramps, pain, or discomfort, mild to moderate; bleeding from rectum; bloated feeling or gas; constipation; diarrhea; fluid retention and edema; headache, mild to moderate; indigestion; nausea; nervousness or irritability

Incidence less frequent

Blurred or double vision or any change in vision; cystitis; decreased appetite or loss of appetite; dizziness; drowsiness; general feeling of discomfort or illness; increased sweating; mental depression; ringing or buzzing in ears; skin rash; stomatitis, aphthous; trouble in sleeping; vomiting

Incidence rare

Agranulocytosis [granulocytopenia]; anaphylaxis or anaphylactoid reactions; anemia, hemolytic; bitter taste or other taste change; bleeding from vagina; blood in urine; bronchospastic allergic reactions; bulbous eruptions/blisters; cardiac arrythmias; confusion; congestive heart failure or exacerbation of; conjunctivitis; decreased hearing or any change in hearing; dermatitis, allergic; dermatitis, exfoliative; dry, irritated, or swollen eyes; erythema or other skin discoloration; eye pain; fast heartbeat; forgetfulness; gastritis; gastrointestinal bleeding, gastrointestinal perforation and/or ulceration; hallucinations; hemoptysis; hepatitis or jaundice, toxic; hives; hypocoagulability; increased blood pressure; interstitial nephritis; irritation, dryness, or soreness of mouth; itching; laryngeal edema, lightheadedness/vertigo; loosening or splitting of fingernails or other nail disorders; migraine; muscle cramps; nephrotic syndrome; neuropathy, peripheral; nosebleeds, unexplained; pancreatitis; photoallergic or photosensitive dermatologic reaction; pounding heartbeat; renal impairment or failure; rhinitis, allergic; shortness of breath or troubled breathing; syncope; thirst, continuing;

thrombocytopenia with or without purpura, trembling or twitching; weight loss, unexplained

Incidence unknown

Abdominal distention; amblyopia, toxic; angioedema; angitis; anxiety; aplastic anemia [pancytopenia]; bladder pain; bone marrow depression; chestpain; cholistatic hepatitis or jaundice; colitis or exacerbation of; convulsions; corneal deposits or opacity; crystalluria, renal calculi, or ureteral obstruction; desquamation; disorientation; disseminated intravascular coagulation; dysarthria (trouble in speaking); dysphagia; dysuria; ecchymosis/bruising; eczema; edema, pulmonary; eosinophilia; epigastric pain; enteritis, regional or exacerbation of; enterocolitis; erythema multiforme; erythema nodosum; esophagitis; feeling of depersonalizaton or muzziness; fever; flushing or hotflashes; frequent urge to urinate; gastroenteritis; gingival ulceration; glomerulitis or glomerulonephritis; glossitis; headache, severe, especially in the morning; heartburn; hyperkalemia; incontinence; leukopenia [neutropenia]; Loeffler syndrome [eosinophilic pneumonitis]; lymphadenopathy; meningitis, aseptic; muscle weakness; nephrosis; oliguria/anuria; palpedral edema; pericarditis; petechia; photophobia; photosensitivity reactions; polyuria; proteinuria; psychotic reaction; renal papillary or tubular nephrosis; retinal or macular disturbances; scotomata; serum sickness-like reaction; Stevens-Johnson syndrome (bleeding or crusting sores on lips; chest pain; fever with or without chills; muscle cramps or pain; retinal hemorrhage; skin rash; sores, ulcers, or white spots in mouth; sore throat); strong-smelling urine; swelling of lips and tongue, syncope; systemic lupus erythematosus [SLE]-like syndrome; toxic epidermal necrolysis; trembling or twitching; unusual weakness with no other signs or symptoms; urethritis or urinary tract infection; vasculitis

Overdose

For more information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer**.

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Calves, nonruminating

With a dose of 9 mg/kg once a day for 6 days:[{R-3}]

Abomasal erosions

Dogs

With a dose of up to 20 mg/kg a day for up to 90 days, mild self-limiting evidence of the following were present:[{R-4}]

Anorexia; diarrhea; melena; weight loss

With a dose of 36 mg/kg a day, clinical signs and histopathology results indicated gastrointestinal, liver, and kidney toxic effects were present.[{R-4}]

Horses

With a dose of 2.2 mg/kg every 8 hours for 12 days:

Erosions or ulcerations, gastric or oral[{R-24}]

With a dose of 33 mg/kg a day for 5 days:

Laminitis[{R-2; 3}]—in one of two horses treated

With a dose of 55 mg/kg a day for 5 days:

Abdominal swelling;[{R-2}] ***depression;***[{R-2}] ***icterus;***[{R-2}] ***inappetence;***[{R-21}] ***recumbency***[{R-3}]

Note: Postmortem findings included gastritis, hepatitis, and nephritis.[{R-2; 3}]

Treatment of overdose

Acute

To decrease absorption—Gastric lavage to remove unabsorbed drug from stomach.

Supportive care—Administration of fluids.

Client Consultation

In providing consultation, consider emphasizing the following selected information:

- Keeping water readily available during the treatment period to avoid dehydration
- Never exceeding the prescribed daily amount without veterinary consultation
- Familiarizing clients with signs that an adverse reaction may be occurring; instructing them to contact their veterinarian and discontinue medication if a reaction is suspected
- Not administering nonsteroidal anti-inflammatory drugs labeled for human use to animals without guidance from a veterinarian; human dosages may be toxic or fatal for animals

Veterinary Dosing Information

The side effects associated with nonsteroidal anti-inflammatory agents (NSAIDs) often make it prudent to treat chronic inflammation with the lowest effective dose over the shortest period of time to control signs.{R-1}

For parenteral dosage forms only

Avoid intra-arterial injection.{R-3; 4}

For perioperative administration

Because NSAIDs can produce renal disturbances in animals prone to them, intravenous fluid therapy can be an appropriate precaution in some animals at risk for renal disease.{R-1} Ketoprofen, like other NSAIDs, may contribute to a decrease in glomerular filtration rate for up to 48 hours when administered before surgery without the benefit of intravenous fluid support.{R-62} Healthy dogs treated with ketoprofen that were not administered fluid therapy during protracted student-performed ovariohysterectomies did, in some cases, develop transient signs of renal trauma, including mild azotemia and urine sediment renal tubular epithelial cells, the first postoperative day; however, the risk was not found to be higher than that seen with other analgesics, such as morphine.{R-66}

Platelet aggregation measured postoperatively is significantly decreased in healthy dogs administered ketoprofen before elective ovariohysterectomy.{R-65} Studies differ on whether buccal mucosal bleeding time (BMBT) is significantly changed by preoperative ketoprofen administration; however, for healthy dogs with no other risk factors, the possibility of bleeding during surgery may be low.{R-62; 65; 68} Concurrent administration of other drugs that inhibit platelet function, such as cephalosporins, should be avoided when ketoprofen is administered preoperatively.{R-63} Preoperative administration of NSAIDs to animals with potential bleeding disorders should be avoided.{R-68}

Treatment of adverse effects

If gastrointestinal signs appear, including decreased appetite, soft stool, or diarrhea, medication should be discontinued until the signs disappear.{R-1} If the adverse effects are mild, medication may be reinitiated at a lower dose, with observation for recurrence of adverse effects.{R-1} If treatment is necessary, misoprostol or sucralfate can be used in the treatment of gastrointestinal ulceration.{R-42}

Oral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

Human products have been listed for this dosage form based on relevance to veterinary practice.

KETOPROFEN CAPSULES

Usual dose: See *Ketoprofen Tablets*.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):[R-49]

25 mg (Rx) [*Orudis* (lactose); GENERIC].

50 mg (Rx) [*Orudis* (lactose); GENERIC].

75 mg (Rx) [*Orudis* (lactose); GENERIC].

Canada—

Veterinary-labeled product(s):[R-4]

Not commercially available.

Human-labeled product(s):[R-49]

50 mg (Rx) [*Apo-Keto; Orudis; Rhodis*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer.

USP requirements: Not in USP.[R-48]

KETOPROFEN EXTENDED-RELEASE CAPSULES

Usual dose:

Note: Bioavailability in animals has not been specifically demonstrated for delayed-release, enteric coated, or extended-release dosage forms developed for human therapy; therefore, these products are not recommended for veterinary use.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):[R-49]

100 mg (Rx) [*Oruvail;* GENERIC].

150 mg (Rx) [*Oruvail*].

200 mg (Rx) [*Oruvail;* GENERIC].

Canada—

Veterinary-labeled product(s):[R-4]

Not commercially available.

Human-labeled product(s):[R-49]

150 mg (Rx) [*Oruvail*].

200 mg (Rx) [*Oruvail*].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

USP requirements: Not in USP.[R-48]

KETOPROFEN TABLETS

Usual dose:

[Fever];

[Musculoskeletal inflammation]; or

[Postsurgical pain]—*Cats* and *dogs:* As stated on Canadian product labeling, oral, 1 mg per kg of body weight every twenty-four hours.[R-4] It is recommended that ketoprofen treatment be limited to a maximum of five consecutive days to reduce the risk of adverse gastrointestinal effects.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):[R-49]

12.5 mg (OTC) [*Orudis KT*].

Canada—

Veterinary-labeled product(s):[R-4]

5 mg (Rx) [*Anafen;* GENERIC].

10 mg (Rx) [*Anafen*].

20 mg (Rx) [*Anafen;* GENERIC].

Human-labeled product(s):

Not commercially available.

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from direct sunlight.{R-4}

USP requirements: Not in USP.{R-48}

KETOPROFEN DELAYED-RELEASE TABLETS

Usual dose:

Note: Bioavailability in animals has not been specifically demonstrated for delayed-release, enteric coated, or extended-release dosage forms developed for human therapy; therefore, these products are not recommended for veterinary use.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):{R-49}

Not commercially available.

Canada—

Veterinary-labeled product(s):{R-4}

Not commercially available.

Human-labeled product(s):

50 mg (Rx) [*Apo-Keto-E; Novo-Keto-EC; Orudis-E; Rhodis-EC;* GENERIC].

100 mg (Rx) [*Apo-Keto-E; Novo-Keto-EC; Orudis-E; Rhodis-EC;* GENERIC].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

USP requirements: Not in USP.{R-48}

KETOPROFEN EXTENDED-RELEASE TABLETS

Usual dose:

Note: Bioavailability in animals has not been specifically demonstrated for delayed-release, enteric coated, or extended-release dosage forms developed for human therapy; therefore, these products are not recommended for veterinary use.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):{R-49}

Not commercially available.

Canada—

Veterinary-labeled product(s):{R-4}

Not commercially available.

Human-labeled product(s):

200 mg (Rx) [*Orudis-SR;* GENERIC].

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

USP requirements: Not in USP.{R-48}

Parenteral Dosage Forms

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

KETOPROFEN INJECTION

Usual dose:

Note: For *cats, dogs,* and *horses,* it is recommended that ketoprofen treatment be limited to a maximum of five consecutive days to reduce the risk of gastrointestinal effects.

Inflammation, musculoskeletal; or

Pain, musculoskeletal —

Horses: Intravenous, 2.2 mg per kg of body weight every twenty-four hours.{R-2}

Note: A controlled study has demonstrated that a dose of 3.63 mg per kg of body weight significantly relieved the pain associated with laminitis in horses for up to twenty-four hours while 2.2 mg per kg of body weight did not.{R-8}

[*Cats*]: As stated on Canadian product labeling, subcutaneous, 2 mg per kg of body weight as a single dose, followed by ketoprofen tablets at a maintenance dose of 1 mg per kg of body weight every twenty-four hours.{R-4} Alternatively, in severe cases, the parenteral dose can be given once a day for up to 3 days.{R-4}

[*Cattle*]: As stated on Canadian product labeling, intramuscular or intravenous, 3 mg per kg of body weight every twenty-four hours for up to three days.{R-3} See also the *Withdrawal times* section below.

[*Dogs*]: As stated on Canadian product labeling, intramuscular, intravenous, or subcutaneous, 2 mg per kg of body weight as a single dose, followed by ketoprofen tablets at a maintenance dose of 1 mg per kg of body weight every twenty-four hours.{R-4} Alternatively, in severe cases, the parenteral dose can be given once a day for up to 3 days.{R-4}

[Fever]—

Cats: As stated on Canadian product labeling, subcutaneous, 2 mg per kg of body weight{R-4} as a single dose, followed by ketoprofen tablets at a maintenance dose of 1 mg per kg of body weight every twenty-four hours.{R-4} Alternatively, in severe cases, the parenteral dose can be given once a day for up to 3 days.{R-4}

Cattle: As stated on Canadian product labeling, intramuscular or intravenous, 3 mg per kg of body weight every twenty-four hours for up to three days.{R-3} See also the *Withdrawal times* section below.

Dogs: As stated on Canadian product labeling, intramuscular, intravenous, or subcutaneous, 2 mg per kg of body weight as a single dose, followed by ketoprofen tablets at a maintenance dose of 1 mg per kg of body weight every twenty-four hours.{R-4} Alternatively, in severe cases, the parenteral dose can be given once a day for up to 3 days.{R-4}

[Inflammation, general];

[Mastitis, acute]; or

[Pain, general]—*Cattle:* As stated on Canadian product labeling, intramuscular or intravenous, 3 mg per kg of body weight every twenty-four hours for up to three days.{R-3; 31} See also the *Withdrawal times* section below.

[Postoperative pain]—

Cats: As stated on Canadian product labeling, subcutaneous, 2 mg per kg of body weight as a single dose, followed by ketoprofen tablets at a maintenance dose of 1 mg per kg of body weight every twenty-four hours.{R-4} Alternatively, in severe cases, the parenteral dose can be given once a day for up to 3 days.{R-4}

Dogs: As stated on Canadian product labeling, intramuscular, intravenous, or subcutaneous, 2 mg per kg of body weight as a single dose, followed by ketoprofen tablets at a maintenance dose of 1 mg per kg of body weight every twenty-four hours.{R-4} Alternatively, in severe cases, the parenteral dose can be given once a day for up to 3 days.{R-4}

[Visceral pain][1]—*Horses:* Intravenous, 2.2 mg per kg of body weight.{R-26; 27} The dose may be repeated in two to twelve hours, depending on clinical signs.{R-26}

Note: [*Calves*][1]—Although the safety and efficacy of ketoprofen have not been established for the treatment of *endotoxemia* in calves, an intramuscular or intravenous dose of 2.2 to 6 mg per kg of body weight has been used, based on efficacy in experimentally induced disease.[{R-14; 30}] See also the *Withdrawal times* section below.

Although the safety and efficacy have not been established in the treatment of *postoperative pain* in calves, an intravenous dose of 3 mg per kg of body weight, administered thirty minutes before surgery, has been suggested, based on controlled studies that recorded behavioral changes and physiologic markers of stress associated with certain procedures.[{R-72-74}] See also the *Withdrawal times* section below.

[*Goats*][1] and [*sheep*][1]—Although the safety and efficacy have not been established for treatment of *inflammatory conditions* in goats and sheep, an intramuscular or intravenous dose of 3 mg per kg of body weight every twenty-four hours for up to three days has been suggested, based on pharmacokinetic data.[{R-43; 47}] See also the *Withdrawal times* section below.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

100 mg per mL (Rx) [*Ketofen*].[{R-2}]

Canada—

Veterinary-labeled product(s):

10 mg per mL (Rx) [*Anafen*].[{R-4}]

100 mg per mL (Rx) [*Anafen*].[{R-3}]

Note: In Canada, the 10-mg-per-mL solution is labeled only for use in cats and dogs, while the 100-mg-per-mL solution is labeled only for use in cattle and horses.[{R-3}]

Withdrawal times:

U.S.—There are no established withdrawal times for animals in the United States because ketoprofen is not labeled for use in food-producing animals.[{R-2}] Under the Animal Medicinal Drug Use Clarification Act (AMDUCA) amendments to the Food, Drug, and Cosmetic Act, a nonsteroidal anti-inflammatory drug that is labeled for use in food-producing animals would be preferred over this product for use in those species.

If ketoprofen is administered to *cattle, goats,* or *sheep* in the United States at a dose of 3.3 mg per kg of body weight every twenty-four hours for up to three days, evidence has been compiled by the Food Animal Residue Avoidance Databank (FARAD) that suggests a meat withdrawal time of 7 days and a milk withholding time of 24 hours would be sufficient to avoid residues.[{R-32; 37-39; 43; 47}]

At this time, there are insufficient data to make a residue withdrawal recommendation for *calves* less than 20 weeks of age that are treated with ketoprofen.

Canada—[{R-3}]

	Withdrawal time
Species	Meat (days)
Cattle	1

Note: Although Canadian product labeling does not specifically list a residue withdrawal time for *milk,* the manufacturer states that there is an established withdrawal of zero hours for cattle; the only indication of this on product labeling is the lack of prohibition from use in lactating dairy cattle.[{R-76}]

Product labeling listing the above withdrawal times states that they apply to a dose of 3 mg per kg of body weight administered every twenty-four hours for up to three days.[{R-3}]

This product is not labeled for use in horses to be slaughtered for food.[{R-3}]

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.{R-2} Protect from direct sunlight.{R-3}

Incompatibilities: Compatability with other medications is unknown; therefore, administration with other medications in the same syringe is not recommended.{R-3}

USP requirements: Not in USP.{R-48}

[1]Not included in Canadian product labeling or product not commercially available in Canada.

Developed: 2/6/04

Table 1. Pharmacology/Pharmacokinetics: Intravenous administration

Note: The commercial forms of ketoprofen contain a racemic mixture of R-(–) and S-(+) enantiomers. In some species, ketoprofen displays enantioselective pharmacokinetics.[R-34; 39] Two kinds of studies are listed in this table. Some studies looked at the pharmacokinetics of each enantiomer after administration of the racemic mixture and others used the administration of each separate enantiomer to investigate the pharmacokinetics for each.[R-33; 39]

Species	Compound administered	Dose (mg/kg)	Compound Assayed	Vd_{area} (L/kg)	Vd_{ss} (L/kg)	Elimination half-life (hours)	Clearance (mL/min·kg)
Camels[R-12]	Ketoprofen*	2	Ketoprofen	0.32	0.13	4.16	1.00
[R-7]	Ketoprofen	2	In females:				
			R(–)	0.12		1.88	0.74
			S(+)	0.14		1.83	0.84
			In males:				
			R(–)	0.22		2.11	1.03
			S(+)	0.23		2.33	1.16
Cattle[R-32; 37]	Ketoprofen	3.3	Ketoprofen		0.11	0.49	2.8
Calves, 20 weeks of age[R-38]	Ketoprofen	1.5	*R*(–)	0.20 ± 0.06		0.42 ± 0.09	5.50 ± 0.50
			S(+)	0.22 ± 0.06		0.42 ± 0.08	5.50 ± 0.67
Calves, 20 weeks of age[R-39]	*R*(–)	1.5	*R*(–)		0.19 ± 0.03	1.30 ± 0.27	2.51 ± 0.60
	S(+)		*S*(+)		0.26 ± 0.04	2.19 ± 0.42	1.98 ± 0.20
Donkeys[R-40]	Ketoprofen	2.2	Ketoprofen		0.26 ± 0.05	1.30 ± 0.75	6.90 ± 1.65
Goats[R-47]	Ketoprofen	2.2	Ketoprofen		0.23 ± 0.05	0.32 ± 0.14	12.3 ± 2.0
Horses							
[R-33]	*R*(–)	1.1	*R*(–)	0.53		1.98	5.77
	S(+)		*S*(+)	0.64		1.09	6.62
[R-19]	Ketoprofen	2.2	*R*(–)	0.47 ± 0.15		1.09 ± 0.19	4.62 ± 0.58
			S(+)	0.49 ± 0.21		1.51 ± 0.45	3.37 ± 0.37
[R-55]	Ketoprofen	2.2	*R*(–)	0.27 ± 0.09	0.17 ± 0.03	0.42 ± 0.18	7.40 ± 1.03
			S(+)	0.16 ± 0.03	0.14 ± 0.02	0.37 ± 0.06	5.27 ± 0.35
[R-56]	Ketoprofen	2.2	*R*(–)		0.48 ± 0.16	1.89 ± 0.82	9.33 ± 1.00
			S(+)		0.22 ± 0.08	1.00 ± 0.50	7.17 ± 1.00
Before induced synovitis[R-35]	Ketoprofen	2.2	Ketoprofen	0.28 ± 0.14	0.14 ± 0.05	1.02 ± 0.47	3.08 ± 0.38
With induced synovitis[R-35]	Ketoprofen	2.2	Ketoprofen	0.20 ± 0.08	0.13 ± 0.03	0.63 ± 0.29	3.66 ± 0.39
With induced synovitis[R-58]	Ketoprofen	2.2	*R*(–)		0.44 ± 0.13	1.87 ± 0.63	6.67 ± 1.17
			S(+)		0.20 ± 0.03	1.14 ± 0.18	3.83 ± 0.67
	R(–)	1.1	*R*(–)		0.79 ± 0.29	2.63 ± 0.81	6.50 ± 0.17
	S(+)	1.1	*S*(+)		0.33 ± 0.13	1.34 ± 0.52	4.83 ± 1.16
Multiple dosing[R-36]	Ketoprofen	2.2 every 12 hours for 5 days	Ketoprofen				
			Day 1		0.16	1.64	4.81
			Day 5		0.18	1.61	4.80
Foals, <24 hours old[R-44]	Ketoprofen	2.2	Ketoprofen	0.39	0.36	4.3	1.03
Llamas[R-20]	Ketoprofen	4.4	*R*(–)	0.10 ± 0.01	0.09 ± 0.01	5.41 ± 0.94	0.21 ± 0.03
			S(+)	0.10 ± 0.01	0.10 ± 0.01	5.49 ± 1.27	0.22 ± 0.03
Sheep							
[R-60]	Ketoprofen	3	*R*(–)		0.17 ± 0.02	0.87 ± 0.10	3.27 ± 0.53
			S(+)		0.26 ± 0.02	0.86 ± 0.08	5.85 ± 0.83
	R(–)	1.5	*R*(–)		0.34 ± 0.05	1.63 ± 0.34	3.87 ± 0.50
	S(+)	1.5	*S*(+)		0.47 ± 0.14	3.23 ± 1.56	4.77 ± 0.98
[R-61]	Ketoprofen	3	*R*(–)		0.11 ± 0.01	0.63 ± 0.05	2.67 ± 0.33
			S(+)		0.18 ± 0.02	0.63 ± 0.05	4.67 ± 0.67
	R(–)	1.5	*R*(–)		0.18 ± 0.04	1.02 ± 0.23	2.67 ± 0.17
	S(+)	1.5	*S*(+)		0.23 ± 0.02	0.94 ± 0.14	5.33 ± 0.33

*In this table, ketoprofen denotes the racemic mixture.

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