Uses/Indications
Finasteride may be useful in treating the benign prostatic hypertrophy in canine patients. Because of the drug's relative expense and the long duration of therapy required to see a response, its usefulness may be limited in veterinary medicine.

It may also be useful in the adjunctive treatment of adrenal disease in ferrets.

Pharmacology/Actions
Finasteride specifically and totally inhibits 5-alpha-reductase. This enzyme is responsible for metabolizing testosterone to dihydrotestosterone (DHT) in the prostate, liver and skin. DHT is a potent androgen and is the primary hormone responsible for the development of the prostate.

Pharmacokinetics
Finasteride is absorbed after oral administration and in humans about 65% is bioavailable. The presence of food does not affect absorption. It is distributed across the blood-brain barrier and is found in seminal fluid. In humans, about 90% is bound to plasma proteins. Finasteride is metabolized in the liver and the half-life is about 6 hours. Metabolites are excreted in the urine and feces. In humans, a single daily dose suppresses DHT concentrations for 24 hours.

Contraindications/Precautions/Warnings
Finasteride is contraindicated in patients hypersensitive to it. It should be used with caution in patients with significant hepatic impairment as metabolism of the drug may be reduced. Finasteride should be used in males only; do not use in sexually developing animals.

Adverse Effects
One study done in dogs reported no adverse effects or irreversibility of effects after treating for 21 weeks at 1 mg/kg. The adverse effects reported in humans have been very limited, mild and transient. Decreased libido, decreased ejaculate volume, and impotence have been reported.

Reproductive/Nursing Safety
In humans, the FDA categorizes this drug as category ***X*** for use during pregnancy (*Studies in animals or humans demonstrate fetal abnormalities or adverse reaction; reports indicate evidence of fetal risk. The risk of use in pregnant women clearly outweighs any possible benefit.*)

Finasteride is not indicated for use in females. It is not known whether finasteride is excreted in milk.

Overdosage/Acute Toxicity
Limited information is available; gastrointestinal effects may be noted.

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

- **ANTICHOLINERGIC DRUGS:** May precipitate or aggravate urinary retention thereby negating the effects of the drug when used for BPH

Doses
- **DOGS:**
  a) For benign prostatic hyperplasia: 0.1–0.5 mg/kg once daily PO; for a 10–50 kg dog, one 5 mg tablet daily (Root Kustritz and Klausner 2000); (Kamolpatana, Johnston et al. 1998), (Bartges 2006c)
  b) For dogs <15 kg: 1.5 mg (approx. ⅓ of a 5 mg tablet); for dogs 15–30 kg = 2.5 mg (½ tablet); for dogs >30 kg = 5 mg (one tablet). Given PO daily. (Romagnoli 2006b)
- **FERRETS:**
  a) For adjunctive treatment of adrenal disease: 5 mg (total dose) tablet once daily (Johnson 2006b)

Monitoring
- Efficacy: Prostate exam

Client Information
- Clients should understand that therapy might be prolonged before efficacy can be determined and regular dosing compliance is mandatory. Once the drug is stopped, the prostate will start growing again.
- Pregnant women should be advised to guard against exposure to this drug as it may cause birth defects.

Chemistry/Synonyms
Finasteride is a 4-azasteroid synthetic drug that inhibits 5 alpha-dihydroreductase (DH), and has a molecular weight of 372.55.

Finasteride may also be known as: finasteridum, MK-0906, and MK-906; many trade names are available.

Storage/Stability
Store tablets below 30°C in tight containers and protected from light.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Finasteride Oral Tablets: 1 mg and 5 mg; *Proscar*®, *Propecia*® (Merck); generic; (Rx)

Fipronil—See the listing in the Dermatological Agents, Topical Appendix

FIROCOXIB

(feer-oh-***koks***-ib) **Previcox®, Equioxx®**

ORAL COX-2 INHIBITOR NSAID

Prescriber Highlights
- **Oral COX-2 NSAID labeled for the control of pain & inflammation associated with osteoarthritis in dogs & horses**
- **Adverse effect profile not fully determined; in DOGS: GI effects (vomiting, anorexia) most likely, but serious effects are possible**
- **Adverse effects in HORSES include mouth ulcers, facial skin lesions, excitation (rare)**

Uses/Indications

Firocoxib is indicated in dogs and horses for the control of pain and inflammation associated with osteoarthritis. A chewable tablet form for dogs and an oral paste for horses are available.

Like other NSAIDs, firocoxib can be useful for treating fever, pain, and/or inflammation associated with other conditions, post-surgery, trauma, etc.

Firocoxib may also be useful in other species, but information is scant regarding its safety and efficacy. One study in cats (McCann, Rickes et al. 2005) evaluating firocoxib in experimentally induced pyrexia, demonstrated that the drug was effective after a single oral dose in preventing or attenuating pyrexia at all doses studied (0.75–3 mg/kg).

Pharmacology/Actions

Firocoxib is a coxib-class, nonsteroidal antiinflammatory drug (NSAID). It is believed to predominantly inhibit cyclooxygenase-2 (COX-2) and spare COX-1 at therapeutic dosages. This theoretically would inhibit production of the prostaglandins that contribute to pain and inflammation (COX-2) and spare those that maintain normal gastrointestinal, platelet and renal function (COX-1). However, COX-1 and COX-2 inhibition studies are done *in vitro* and do not necessarily correlate perfectly with clinical effects seen in actual patients.

Pharmacokinetics

In dogs, firocoxib absorption after oral dosing varies among individuals. Oral bioavailability with the chewable tablets, on average, is about 38%. Food will delay, but not affect the amount absorbed. Peak levels occur about 1 hour after dosing if fasted, and 5 hours if the patient is fed. Volume of distribution at steady state is about 3 L/kg; it is 96% bound to plasma proteins. Biotransformation occurs predominantly via dealkylation and glucuronidation in the liver; elimination is principally in the bile and feces. Elimination half-life in dogs is approximately 6–8 hours.

In horses, oral availability after administering the paste is approximately 79%. Peak levels occur 4–12 hours after dosing. Volume of distribution at steady state is about 1.7 L/kg and it is 98% bound to plasma proteins. Biotransformation in horses occurs primarily via decyclopropylmethylation and then glucuronidation. Metabolites are primarily excreted in the urine. Elimination half-life is approximately 30–40 hours.

Pharmacokinetics of firocoxib have only been reported in two cats studied (McCann, Rickes et al. 2005). Oral bioavailability after administering an oral suspension was about 60% and the volume of distribution, between 2–3 L/kg. Elimination half-life in the two cats studied averaged about 10 hours.

Contraindications/Precautions/Warnings

Firocoxib should not be used in animals hypersensitive to it or other NSAIDs. The drug should be used with caution and enhanced monitoring in patients with preexisting renal, hepatic or cardiovascular dysfunction, and those that are dehydrated, hypovolemic, hypotensive, or on concomitant diuretic therapy. Because geriatric patients have reduced renal function and firocoxib is often used for osteoarthritis in this patient population, ongoing monitoring for adverse effects is mandatory.

Because all NSAIDs can potentially cause GI toxicity, firocoxib is relatively contraindicated in dogs with active GI ulcerative conditions. As it may affect platelet function, it is relatively contraindicated in patients with bleeding disorders or thrombocytopenia.

The safety of firocoxib in horses less than one year old has not been established.

A chronic dosing (5 mg/kg for 6 months) study performed in puppies 10–13 weeks old, showed subclinical periportal hepatic fatty changes in half the dogs studied. Higher doses (15–25 mg/kg; 3–5X) in this age range caused increased rates of hepatic fatty changes; some dogs died or were euthanized due to moribund conditions. The manufacturer states in the package insert: "Use of this product at doses above the recommended 5 mg/kg in puppies less than 7 months old has been associated with serious adverse reactions, including death" and "…this product cannot be accurately dosed in dogs weighing less than seven pounds in body weight." The labeling in the UK states that it should not be used in dogs "less than 10 weeks of age."

If changing from one NSAID to another in dogs for reasons of efficacy, consider a washout period between agents. While the actual length of time between agents is controversial and opinions vary widely, often a 24-hour washout period between COX-2 selective agents is recommended. Recommendations for washout periods before starting a COX-2 selective agent after using a non-selective agent or aspirin are usually much longer (72 hours–1 week).

Adverse Effects

Because firocoxib is a relatively new product, its adverse effect profile in dogs is yet to be fully determined. In pre-approval studies (128 dogs treated), vomiting and decreased appetite/anorexia were the most common adverse effects noted with an approximate incidence rate of 4% and 2%, respectively.

In the FDA's CVM Cumulative Adverse Drug Experiences (ADE) Summaries Report (through 12/06/2006) for firocoxib in dogs, the most prevalent ADE reported was vomiting. On the list of 10 most reported ADE's for firocoxib, the second most reported event was anorexia. Other effects on this list included: diarrhea, increases in BUN, creatinine, alkaline phosphatase and ALT, depression/lethargy, and ataxia. Melena, GI ulcers, bloody vomiting and GI perforation were included within the 25 most reported events listed. It should be noted that this data reflects voluntary reporting to the FDA and does not reflect actual incidence rates, nor is causation necessarily proven.

In pre-approval studies done in horses treated for 14 days, diarrhea/loose stools were seen in about 2%. Excitation was rarely (<1%) detected. In safety studies, oral lesions/ulcers were seen in some horses after dosages of 1–5X were given.

Reproductive/Nursing Safety

Information on the safety of firocoxib in breeding, pregnant or lactating dogs or horses is not available. Studies performed in pregnant rabbits at dosages approximating those given to dogs, demonstrated maternotoxic and fetotoxic effects.

Overdosage/Acute Toxicity

Limited information is available for acute overdoses in animals. The reported oral LD50 for rats is > 2 grams per kg. Should an overdose occur, contacting an animal poison control center or the manufacturer (1-877-217-3543) is highly recommended. Use of gut emptying protocols and supportive treatment (IV fluids, oral sucralfate, etc.) may be useful in managing the case.

Drug Interactions

In the package insert for *Previcox*, the manufacturer states the following (**Note: bold** mine—Plumb): "As a class, cyclooxygenase inhibitory NSAIDs may be associated with renal and gastrointestinal toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. 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 antiprostaglan-

din effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since many NSAIDs possess the potential to produce gastrointestinal ulcerations, concomitant use with other antiinflammatory drugs, such as **NSAIDs** or **corticosteroids**, should be avoided or closely monitored. The concomitant use of **protein bound drugs** with PREVICOX™ Chewable Tablets 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 the metabolism of PREVICOX™ Chewable Tablets has not been evaluated."

Drug interactions reported in humans taking NSAIDS, that may be of significance in veterinary patients receiving firocoxib include:

- **ACE INHIBITORS** (*e.g.,* **enalapril, benazepril**): Some NSAIDs can reduce effects on blood pressure
- **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 firocoxib levels in dogs
- **FUROSEMIDE**: NSAIDs may reduce the saluretic and diuretic effects
- **HIGHLY PROTEIN BOUND DRUGS** (**phenytoin, valproic acid, oral anticoagulants, other antiinflammatory agents, salicylates, sulfonamides, sulfonylurea antidiabetic agents**): As firocoxib is highly bound to plasma proteins (95–98%), it may displace other highly bound drugs or these agents could displace firocoxib. Increased serum levels, duration of actions and toxicity could occur.
- **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 development

Laboratory Considerations

No specific laboratory concerns; see Monitoring

Doses

- **DOGS:**

  For the control of pain and inflammation associated with osteoarthritis (labeled indication):

  a) 5 mg/kg (2.27 mg/lb) PO once daily. Dosage should be calculated in half tablet increments and can be administered with or without food. (Package insert; *Previcox*®—Merial)

- **CATS:**

  Caution: While firocoxib may ultimately be shown to be safe for use in cats, supporting information (or FDA approval) is not currently available for it to be recommended.

- **HORSES:**

  For the control of pain and inflammation associated with osteoarthritis (labeled indication):

  a) 0.1 mg/kg (0.45 mg/lb) body weight PO daily for up to 14 days (Package insert; *Equioxx*®—Merial)

Monitoring

- Baseline and periodic physical exam including clinical efficacy and adverse effect queries
- Baseline and periodic: CBC, liver function, renal function, and electrolytes; urinalysis

Client Information

- The manufacturer provides a client hand-out that is recommended to be distributed each time the drug is dispensed
- May be administered with or without food
- Contact veterinarian if any of the following occur in dogs: vomiting, decreased appetite/weight loss, diarrhea or loose stools, changes in behavior or activity, changes in water consumption or urination, or yellowing of whites of eyes or mucous membranes
- For horses, contact veterinarian if patient develops ulcers or sores on tongue or in mouth, sores or lesions on facial skin or lips, diarrhea/loose stools, changes in behavior/activity, changes in feed or water consumption, or yellowing of whites of eyes or mucous membranes

Chemistry/Synonyms

Firocoxib occurs a white crystalline powder.

Firocoxib may also be known as: 3-(cyclopropylmethoxy)-5, 5-dimethyl-4-(4-methylsulfonyl) phenylfuran-2(5H)-on or ML-1,785,713, *Equioxx*®, and *Previcox*®.

Storage/Stability/Compatibility

Commercially available tablets and oral paste should be stored at room temperature (15–30°C); brief excursions are permitted up to 40°C (104°F).

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Firocoxib Chewable Tablets (scored): 57 mg, & 227 mg; *Previcox*® (Merial); (Rx). Approved for use in dogs.

Firocoxib Oral Paste: 0.82% w/w (8.2 mg firocoxib per gram of paste) in a 6.93 gram oral syringe (total of 56.8 mg of firocoxib per syringe); *Equioxx*® (Merial); (Rx).

HUMAN-LABELED PRODUCTS: None

Fish Oil—See Fatty Acids

FLAVOXATE HCL

(fla-*vox*-ate) Urispas®

PARASYMPATHETIC BLOCKER; URINARY ANTISPASMODIC

Prescriber Highlights

- Alternative medication to treat with detrusor hyperspasticity (hyperactive bladder; urge incontinence) in dogs
- Not commonly used; little information available on veterinary use
- Most likely adverse effect is weakness

Uses/Indications

Flovoxate may be considered for treating dogs with detrusor hyperspasticity (hyperactive bladder, urge incontinence).

Pharmacology/Actions

Flavoxate has direct smooth muscle relaxing properties and antimuscarinic effects.