■ **CATS:**

For FeLV-induced anemia or as a general bone marrow stimulant:

a) 10–20 mg IM once weekly (is of questionable benefit) (Maggio-Price 1988)

For chronic anemia secondary to feline cardiomyopathy:

a) 50 mg IM weekly (Harpster 1986)

■ **REPTILES:**

To reduce protein catabolism in renal disease of lizard species:

a) 1 mg/kg IM every 7–28 days (de la Navarre 2003a)

Monitoring

- Androgenic side effects
- Fluid and electrolyte status, if indicated
- Liver function tests if indicated
- Red blood cell count, indices, if indicated
- Weight, appetite

Client Information

- Because of the potential for abuse of anabolic steroids by humans, this agent is a controlled (C-III) drug. It should be kept in a secure area and out of the reach of children.

Chemistry/Synonyms

An injectable anabolic steroid, nandrolone decanoate occurs as a white, to creamy white, crystalline powder. It is odorless or may have a slight odor and melts between 33–37°C. Nandrolone decanoate is soluble in alcohol and vegetable oils and is practically insoluble in water. The commercially available injectable products are generally solutions dissolved in sesame oil.

Nandrolone decanoate may also be known as: nortestosterone decanoate, or nortestosterone decylate.

Storage/Stability/Compatibility

Nandrolone decanoate for injection should be stored at temperatures less than 40°C and preferably between 15–30°C (59–86°F); protect from freezing and light.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 4 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Nandrolone Decanoate Injection (in oil): 100 mg/mL in 2 mL multidose vials & 200 mg/mL in 1 mL vials; generic; (Watson); (Rx, C-III)

NAPROXEN

(na-***prox***-en) Naprosyn®, Aleve®

NONSTEROIDAL ANTIINFLAMMATORY AGENT

Prescriber Highlights

- NSAID; use largely superceded by newer, less GI-toxic NSAIDs in dogs & by other NSAIDs in horses as the equine product is no longer marketed (in USA)
- Contraindications: Active GI ulcers or history of hypersensitivity to the drug. Relatively Contraindicated: Hematologic, renal or hepatic disease. Caution: History of gastric ulcers, heart failure
- Because of difficulty in accurately dosing, adverse effects, & safer alternatives, usually not used in dogs
- Adverse Effects: Relatively uncommon in HORSES: Possible GI (distress, diarrhea, ulcers), hematologic (hypoproteinemia, decreased hematocrit), renal (fluid retention), & CNS (neuropathies) DOGS: GI ulcers & perforation, renal effects (nephritis/nephrotic syndrome), & hepatic (increased liver enzymes) effects
- Drug Interactions

Uses/Indications

The manufacturer lists the following indications: "…for the relief of inflammation and associated pain and lameness exhibited with myositis and other soft tissue diseases of the musculoskeletal system of the horse." (Package Insert; *Equiproxen*®—Syntex). It has also been used as an antiinflammatory/analgesic in dogs for the treatment of osteoarthritis and other musculoskeletal inflammatory diseases (see adverse reactions below).

Pharmacology/Actions

Like other NSAIDs, naproxen exhibits analgesic, antiinflammatory, and antipyretic activity probably through its inhibition of cyclooxygenase with resultant impediment of prostaglandin synthesis.

Pharmacokinetics

In horses, the drug is reported to have a 50% bioavailability after oral dosing and a half-life of approximately 4 hours. Absorption does not appear to be altered by the presence of food. It may take 5–7 days to see a beneficial response after starting treatment. Following a dose, the drug is metabolized in the liver. It is detectable in the urine for at least 48 hours in the horse after an oral dose.

In dogs, absorption after oral dosing is rapid and bioavailability is between 68–100%. The drug is highly bound to plasma proteins. The average half-life in dogs is very long at 74 hours.

In humans, naproxen is highly bound to plasma proteins (99%). It crosses the placenta and enters milk in levels of about 1% of those found in serum.

Contraindications/Precautions/Warnings

Naproxen is relatively contraindicated in patients with a history of or preexisting hematologic, renal, or hepatic disease. It is contraindicated in patients with active GI ulcers, or with a history of hypersensitivity to the drug. It should be used cautiously in patients with a history of GI ulcers, or heart failure (may cause fluid retention). Animals suffering from inflammation secondary to concomitant infection, should receive appropriate antimicrobial therapy.

Adverse Effects

Adverse effects are apparently uncommon in horses. The possibility exists for GI (distress, diarrhea, ulcers), hematologic (hypoproteinemia, decreased hematocrit), renal (fluid retention), and CNS (neuropathies) effects.

Reports of GI ulcers and perforation associated with naproxen have occurred in dogs. Dogs may also be overly sensitive to the adverse renal (nephritis/nephrotic syndrome) and hepatic effects (increased liver enzymes) of naproxen. Because of the apparently very narrow therapeutic index and the seriousness of the potential adverse reactions that can be seen in dogs, many clinicians feel that the drug should not be used in this species.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*) In studies in rodents and in limited studies in horses, no evidence of teratogenicity or adverse effects in breeding performance have been detected following the use of naproxen. Weigh the potential benefits of therapy against the potential risks of its use in pregnant animals.

Most NSAIDs are excreted in maternal milk. Naproxen appears at approximately 1% of maternal serum concentration.

Overdosage/Acute Toxicity

There is very limited information regarding acute overdoses of this drug in humans and domestic animals. The reported oral LD_{50} in dogs is >1000 mg/kg.

One report of a dog that received 5.6 mg/kg for 7 days has been published (Gilmour and Walshaw 1987). The dog presented with clinical signs of melena, vomiting, depression, regenerative anemia, and pale mucous membranes. Laboratory indices of note included neutrophilia with a left shift, BUN of 66 mg/dl, serum creatinine of 2.1 mg/dl, serum protein to albumin of 4.0:2.1 g/dl. The dog recovered following treatment with fluids/blood, antibiotics, vitamin/iron supplementation, oral antacids, and cimetidine.

There were 236 exposures to naproxen reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases 213 were dogs with 35 dogs showing clinical signs and the remaining 22 cases were cats with 4 cats showing clinical signs. Common findings in dogs recorded in decreasing frequency included vomiting, bloody diarrhea, melena, ataxia and diarrhea. Common findings in cats recorded in decreasing frequency included vomiting, azotemia, bloody vomitus, facial twitching and hypothermia.

As with any NSAID, overdosage can lead to gastrointestinal and renal effects. Decontamination with emetics and/or activated charcoal is appropriate. For doses where GI effects are expected, the use of gastrointestinal protectants is warranted. If renal effects are also expected, fluid diuresis should be considered. Supportive treatment should be instituted as necessary. Monitor electrolyte and fluid balance carefully and manage renal failure using established guidelines.

Drug Interactions

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

- **AMINOGLYCOSIDES** (**gentamicin, amikacin,** etc.): Increased risk for nephrotoxicity
- **ANTICOAGULANTS** (**heparin, LMWH, warfarin**): Increased risk for bleeding possible
- **ASPIRIN**: When aspirin is used concurrently with naproxen, plasma levels of naproxen could decrease and an increased likelihood of GI adverse effects (blood loss) could occur. Concomitant administration of aspirin with naproxen cannot be recommended.
- **BISPHOSPHONATES** (**alendronate,** etc.): May increase risk for GI ulceration
- **CORTICOSTEROIDS**: Concomitant administration with NSAIDs may significantly increase the risks for GI adverse effects
- **FUROSEMIDE**: Naproxen may reduce the saluretic and diuretic effects of furosemide
- **HIGHLY PROTEIN BOUND DRUGS** (*e.g.,* **phenytoin, valproic acid, oral anticoagulants, other antiinflammatory agents, salicylates, sulfonamides,** and the **sulfonylurea antidiabetic agents**): Because naproxen is highly bound to plasma proteins (99%), it potentially could displace other highly bound drugs; increased serum levels and duration of actions may occur. Although these interactions are usually of little concern clinically, use together with caution.
- **METHOTREXATE**: Serious toxicity has occurred when NSAIDs have been used concomitantly with methotrexate; use together with extreme caution.
- **PROBENECID**: May cause a significant increase in serum levels and half-life of naproxen.

Doses

- **DOGS:**

  Note: Because of the difficulty in accurately dosing naproxen and its potential for adverse effects, the use of this drug in dogs should only be considered when approved and safer NSAIDs have been ineffective.

  a) 2 mg/kg PO every other day (q48h) (Hansen 2003b), (Hardie, Lascelles et al. 2003), (Hardie and Grauer 2007)

- **RABBITS, RODENTS, SMALL MAMMALS:**

  a) Rabbits: For septic arthritis pain; inflammation: 2.4 mg/mL in drinking water for 21 days (Ivey and Morrisey 2000)

- **HORSES:**(**Note:** ARCI UCGFS Class 4 Drug)

  a) 5 mg/kg by slow IV, then 10 mg/kg, PO (top dressed in feed) twice daily for up to 14 days or 10 mg/kg, PO (top dressed in feed) twice daily for up to 14 consecutive days. (Package Insert; *Equiproxen*®—Syntex Animal Health; **Note:** No longer commercially available)

  b) 10 mg/kg PO daily (Trumble and Kawcak 2003)

Monitoring

- Analgesic/antiinflammatory efficacy
- GI: appetite, feces (occult blood, diarrhea)
- PCV (packed cell volume), hematocrit if indicated or on chronic therapy
- WBC's if indicated or on chronic therapy

Client Information

- Notify veterinarian if clinical signs of GI distress (anorexia, vomiting, diarrhea, black feces, or blood in stool) occur, or if animal becomes depressed.

Chemistry/Synonyms

Naproxen is a propionic acid derivative, having similar structure and pharmacologic profiles as ibuprofen and ketoprofen. It is a white to off-white crystalline powder with an apparent pK_a of 4.15. It is practically insoluble in water and freely soluble in alcohol. The sodium salt is also available commercially for human use.

Naproxen may also be known as: naproxeneum, RS-3540, RS-3650, *Aleve®*, *Anaprox®*, *EC-Naprosyn®*, *Midol®*, *Naprelan®* and *Naprosyn®*.

Storage/Stability/Compatibility

Naproxen should be stored in well-closed, light resistant containers at room temperature. Temperatures above 40° C (104°F) should be avoided.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

None; the equine product is no longer marketed in the USA.

The ARCI (Racing Commissioners International) has designated this drug as a class 4 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Naproxen Tablets: 200 mg (220 mg naproxen sodium), 250 mg (275 mg naproxen sodium), 375 mg, 500 mg (550 mg naproxen sodium); *Naprosyn®* (Roche); *Anaprox®* and *Anaprox DS®* (Roche); *Aleve®* & *Midol® Extended Relief* (Bayer); generic; (Rx and OTC)

Naproxen Delayed/Controlled-release Tablets: 375 mg) & 500 mg; *EC-Naprosyn®* (Roche); *Naprelan®* (Blansett Pharmacal); generic; (Rx)

Naproxen Oral Suspension: 125 mg/5 mL in 15 mL, 20 mL, 473 mL & 500 mL; *Naprosyn®* (Roche); generic; (Rx)

NARCOTIC (OPIATE) AGONIST ANALGESICS, PHARMACOLOGY OF

Receptors for opiate analgesics are found in high concentrations in the limbic system, spinal cord, thalamus, hypothalamus, striatum, and midbrain. They are also found in tissues such as the gastrointestinal tract, urinary tract, and in other smooth muscle.

Opiate receptors are further broken down into five main subgroups. *Mu* receptors are found primarily in the pain regulating areas of the brain. They are thought to contribute to the analgesia, euphoria, respiratory depression, physical dependence, miosis, and hypothermic actions of opiates. *Kappa* receptors are located primarily in the deep layers of the cerebral cortex and spinal cord. They are responsible for analgesia, sedation, and miosis. *Sigma* receptors are thought to be responsible for the dysphoric effects (struggling, whining), hallucinations, respiratory and cardiac stimulation, and mydriatic effects of opiates. *Delta* receptors, located in the limbic areas of the CNS, and epsilon receptors have also been described, but their actions have not been well explained at this time.

The morphine-like agonists (morphine, meperidine, oxymorphone) have primary activity at the *mu* receptors, with some activity possible at the *delta* receptor. The primary pharmacologic effects of these agents include: analgesia, antitussive activity, respiratory depression, sedation, emesis, physical dependence, and intestinal effects (constipation/defecation). Secondary pharmacologic effects include, *CNS*: euphoria, sedation, and confusion. *Cardiovascular:* bradycardia due to central vagal stimulation, alpha-adrenergic receptors may be depressed resulting in peripheral vasodilation, decreased peripheral resistance, and baroreceptor inhibition. Orthostatic hypotension and syncope may occur. *Urinary:* Increased bladder sphincter tone can induce urinary retention.

Various species may exhibit contradictory effects from these agents. For example, horses, cattle, swine, and cats may develop excitement after morphine injections and dogs may defecate after morphine. These effects are in contrast to the expected effects of sedation and constipation. Dogs and humans may develop miosis, while other species (especially cats) may develop mydriasis. For more information see the individual monographs for each agent.

N-BUTYLSCOPOLAMMONIUM BROMIDE (HYOSCINE BUTYLBROMIDE)

(en-***byoo***-tel-skoe-***pahl***-ah-***moe***-nee-um ***broe***-mide)

Buscoban®

QUATERNARY AMMONIUM ANTISPASMODIC & ANTICHOLINERGIC

Prescriber Highlights

- **Injectable anticholinergic used in horses for treating colic associated with spasmodic colic, flatulent colic, & simple impactions**
- **Shorter acting than atropine; only labeled for a single (one-time) dose IV**
- **Not for use in patients with ileus or when decreased GI motility may be harmful**
- **Adverse effects include transient tachycardia, pupil dilation, decreased secretions & dry mucous membranes**

Uses/Indications

N-butylscopolammonium bromide injection is indicated (per the label) for control of abdominal pain (colic) associated with spasmodic colic, flatulent colic, and simple impactions in horses. It may also be of benefit as an aid to performing rectal exams in horses.

Pharmacology/Actions

N-butylscopolammonium reduces gastrointestinal peristalsis and rectal pressure via its anti-cholinergic actions by competitively inhibiting muscarinic receptors on smooth muscle. N-butylscopolammonium has shorter duration of action than atropine.

Pharmacokinetics

Limited information is available for horses. After an intravenous dose, the drug is eliminated within 48 hours in urine and feces equally. Estimated elimination half-life is approximately 6 hours.

Contraindications/Precautions

N-butylscopolammonium is labeled as contraindicated in horses with impaction colics associated with ileus or those with glaucoma.

This medication is not to be used in horses intended for food purposes.

The manufacturer has not studied the safety of IM administration.