National Cutting Horse Association

Medication Factsheet:

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Permitted Medications:

Non-steroids anti-inflammatory medications

Introduction

The current uses and common diseases of horses predispose them to conditions of pain and inflammation. Inflammation is common to all injured body tissues and the basic response is the same irrespective of the cause of the injury. The clinical signs associated with inflammation have been described in medical literature for thousands of years. While it may be difficult to appreciate redness in pigmented or hair covered skin, swelling with heat, pain and loss of function are easily recognized in inflammatory conditions in the horse. The demands of competitive riding result in many inflammatory conditions of the musculoskeletal system. The nature of the work that horses perform causes sprains and strains, and in some cases, failure of ligaments, tendons, joints and bone, which may lead to temporary or permanent disability.

Inflammation is the body's defense mechanism against tissue injury and usually leads to successful tissue healing. In some cases, the inflammatory process itself actually causes further injury. In order to accelerate healing it may be appropriate to intercede with analgesic (pain-killing) and anti-inflammatory medications. There are several categories of therapeutic medication that mitigate pain and inflammation in horses. The non-steroidal anti-inflammatory drugs act predominantly at the site of injury to control inflammation and in that way help manage pain due to inflammation.

Arachidonic acid pathways

Inflammation is a primary cellular response to an insult or injury from bacteria or other organisms, as well as chemical and physical insults. Arachidonic acid is a fatty acid component of the phospholipid membrane of cells. When the cell membrane is injured, the enzyme phospholipase A2 cleaves arachidonic acid from its position in the cell membrane. Once released from the cell membrane, arachidonic acid is further acted on by cyclooxygenase (COX) or lipoxygenase (LOX) enzymes, through cyclic and linear pathways. When cyclooxygenase acts on arachidonic acid, the end result is the formation of prostaglandins, thromboxane and prostacyclin. These chemicals have potent effects on the vascular system. In some circumstances, their biologically opposite effects, are exploited to provide a "check and balance" system that maintains normal blood vessel muscle tone promoting hemostasis. In inflammatory conditions, this "balance" can be decline or disappear all together. The effects of prostacyclin are seen first, causing increased blood flow to the damaged area from dilation of blood vessels. The increased blood flow increases the supply of nutrients, oxygen, antibodies, white blood cells and other defensive substances to the site of injury. Swelling, heat and reddening results from the increased blood flow and from leaking of blood fluids into the surrounding tissues. Further on in the inflammatory process, thromboxane and prostaglandin activity dominates, resulting in widespread vasoconstriction, pain, fever, platelet clumping and formation of thrombi (blood clots), and reduced oxygen delivery to the tissues.

Pharmacology
The NSAIDs commonly used in horses are:

- Phenylbutazone
- Flunixin meglumine
- Diclofenac
- Ketoprofen
- Firocoxib
- Meclofenamic acid
- Naproxen

All NSAIDs are weak acids and highly bound to proteins in the blood. Therefore, they are well absorbed from the stomach were the pH is normally more acidic, but then because of protein binding, most of the drug remains in the blood. Only low levels of NSAIDs are found in normal tissues and joint fluid. In damaged tissues and joints however, NSAID levels may increase to therapeutic levels because of the increased blood flow and the leaking of blood fluids from damaged blood vessels.

Mechanism of action
The NSAIDs block the COX enzyme, interrupting formation of thromboxane, prostacyclin and the prostaglandins from arachidonic acid. This results in antipyretic action (reduces fever), mild pain relief, anti-inflammatory effects and inhibition of platelet clumping. Recent research has also shown that some of the NSAIDs act on pain receptors in the central nervous system and block pain in the same way as drugs like morphine.

Drug interactions
The occurrence and potential hazards of drug interactions must be considered with therapeutic use of the NSAIDs. In general, any two NSAIDs administered together will be additive in their effect. Since all NSAIDs act by the same mechanism of COX inhibition, higher dose of a single NSAID should produce the same response.

Because all of the NSAID drugs are highly bound to blood proteins, caution must be used when other highly protein bound drugs are administered. Competition for protein binding sites can result in dramatic increases in free drug available for pharmacological action and cause toxicity.

Adverse effects:
The adverse effects of the NSAIDs are related to blocking COX in tissues where prostaglandins are beneficial and protective. Reduction in protective prostaglandins results in constriction of blood vessels and tissue damage in the kidney and reduction in blood flow and protective mucus production in the gastrointestinal tract resulting in ulcers, colic and diarrhea. NSAIDs have a higher incidence of toxicity in foals because their kidney function is not fully developed. NSAIDs should be administered very cautiously to dehydrated horses. Blood concentrations will be greater than normal in the dehydrated horse and are more likely to cause toxicity.

Phenylbutazone ("Bute", PBZ)

Pharmacology:
Phenylbutazone (Bute) has analgesic (pain relieving), anti-inflammatory, and antipyretic (fever

reducing) activity from inhibition of COX. It is available in many intravenous and oral formulations (powder, paste, tablets). The injectable formulation must be given by careful intravenous injection, otherwise it causes severe tissue damage if given intramuscularly or subcutaneously. Following oral administration, Bute is well absorbed, but the time it takes to reach peak blood levels is delayed by feeding the horse, as the Bute sticks to feed particles. In the blood, greater than 99% of the Bute is carried bound to blood proteins. Phenylbutazone is converted by P450 enzymes in the liver to oxyphenbutazone, a metabolite with the same action as Bute, but removed slower from the body than Bute. The capacity of the liver to process Bute becomes overwhelmed at relatively low drug doses. Therefore, increasing doses of Bute can easily result in toxicity. In the horse, the therapeutic effect of Bute lasts for more than 24 hours, due to the slow excretion of the oxyphenbutazone an active metabolite.

Uses/indications:
Phenylbutazone is used extensively in horses for a variety of common musculoskeletal disorders including navicular disease, laminitis, osteoarthritis and degenerative joint disease. It is economical and many brands are available. The use of Bute in performance horses is is highly regulated by individual performance associations. It is less effective in the therapy of colic and endotoxemia than flunixin meglumine (Banamine®). An initial dose of 4.4 mg/kg every 12 hours for the first day of therapy is followed by 2.2 mg/kg once a day for several days. Due to drug accumulation from the slow excretion of oxyphenbutazone, long-term Bute therapy for chronic lameness conditions should be on an every other day basis with the lowest effective dose.

Adverse effects:
Gastrointestinal effects are the most important adverse effects of Bute therapy in horses. Clinical signs include loss of appetite, depression, colic, weight loss, and diarrhea. Hemorrhages and ulcers may occur in the mouth, esophagus, stomach, cecum and colon. These toxic effects are related to the dose of Bute administrated. Horses that receive less than 0.4 g/l00 lbs of body weight per day for 4 days (4 grams to a 1000 lb horse) or 0.1-0.2 g/100 lbs of body weight per day for up to 50 days remain clinically normal. Horses that receive more than 0.4 g/100 lbs of body weight per day for 4 days develop toxicity. In a study, horses that received approximately 7 g of Bute developed gastrointestinal ulcers within 24 hours. Ulcer formation is thought to be predominantly due to Bute -induced blood vessel constriction to the mucosal lining of the gastrointestinal tract. Bute also causes kidney damage from inhibiting the prostaglandins that maintain kidney blood flow. Because of its mechanism of action against prostaglandins, Bute toxicity occurs regardless of the route of administration. Dehydration contributes to the toxicity potential of Bute by reducing the blood flow to the kidney, therefore it is very important that horses on Bute therapy have adequate water intake.
Since normal liver function is required for elimination of Bute, liver disease can result in toxicity even when Bute is administered at recommended doses.

Withdrawal:
Phenylbuazone is eliminated by the kidneys, and can be measured in urine for 7-10 days after a single dose. NCHA does not consider the finding of Bute in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 15 ug/ml. When Bute is administered the dose should be accurately calculated according to the actual weight of the horse at 4 mg/kg. Each 24 hours, not more than 2.0 milligrams per pound of body weight should be administered. <u>For a 1,000-pound horse, the maximum daily dose is 2.0 grams, which equals two 1.0 gram tablets, or two 1.0 gram units of paste, or 10.0 cc of the injectable (200 milligrams per milliliter). No part of a dose should be administered during the 6 hours prior to competing.</u>

Flunixin Meglumine (Banamine®)

Pharmacology:
Flunixin meglumine is a very potent inhibitor of COX that is available in injectable, oral paste and oral granule formulations. Flunixin is rapidly absorbed following oral administration, and peak blood levels occur within 30 minutes. The onset of anti-inflammatory and analgesic action is within 2 hours and duration of action can be up to 36 hours. Flunixin's pain relieving effect lasts long after the concentrations in the blood have become negligible. The long duration of pain relief appears to be due inhibition of inflammatory mediators in tissues.

Uses/indications:
Flunixin is used in horses for a variety of inflammatory and painful conditions: colic, colitis, exertional rhabdomyolysis ("tying up"), endotoxic shock, respiratory disease, eye injuries and diseases, general surgery, laminitis, and other musculoskeletal disorders. Extensive research substantiates the efficacy of flunixin over other NSAIDs in the therapy of endotoxic shock in horses. The recommended dose is 0.25-1.1 mg/kg of body weight once daily, but your veterinarian may need to increase the frequency of this dose in very painful. conditions such as colic. Low dose therapy with flunixin, at one quarter the label dose administered three to four times a day, has anti-endotoxic effects without masking signs of colic pain or causing toxicity. Conversely, extremely high doses of flunixin may mask signs of surgical colic pain and prevent the veterinarian from recognizing the need for surgical intervention. Flunixin does affect normal platelet function, but blood clotting failure is not seen with clinical use and administration prior to surgery is safe.

Adverse effects:
Flunixin has similar adverse effects as Bute, but appears somewhat less toxic than Bute in horses. High doses can result in loss of appetite, depression, and gastrointestinal tract ulcers. In normal foals, the label dose of flunixin administered for 5 days did not produce adverse effects, but six times the label dose resulted in gastrointestinal ulcers. In another study, where foals were administered flunixin at the label dose for 30 days, all treated foals developed gastric ulcers. At three times the label dose given for 7 days, approximately 50% of normal horses or ponies will develop gastric ulcers.

Withdrawal:
Flunixin is eliminated by the kidneys, and can be measured in urine for 3 days after a single dose. NCHA does not consider the finding of flunixin in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 2.0 μg/ml. When flunixin is administered the dose should be accurately calculated according to the actual weight of the horse at 1.1 mg/kg. Each 24 hours, not more than 0.5 milligrams per pound of body weight should be administered. For a 1000 lb. horse, the maximum daily dose is 500 milligrams, which equals two 250-milligram packets of granules, or one 500-milligram packet of granules, or 500 milligrams of the oral paste (available in 1,500-milligram dose syringes), or 10.0 cc of the injectable (50 milligrams per milliliter). No part of a dose should be administered during the 6 hours prior to competing.

Ketoprofen (Ketofen®)

Pharmacology:

Ketoprofen is a propionic acid derivative NSAID. Initial work suggested that ketoprofen had an inhibitory action on LOX in addition to COX inhibition. However, clinical work in horses has shown that ketoprofen principally blocks the production of COX derived mediators of inflammation. Ketoprofen and its active metabolites persist in inflamed tissues at concentrations higher than blood concentrations, so the anti-inflammatory effects of ketoprofen are not related to its concentration in the blood. Ketoprofen is rapidly eliminated from the blood, therefore kidney-damaging drug accumulation does not occur. The maximum anti-inflammatory effects of ketoprofen occur at 12 hours after a dose and last for 24 hours.

Uses/indications:
Ketoprofen is a potent pain reliever, fever reducer, and anti-inflammatory medication. It is often prescribed for soft tissue injury, bone and joint problems, or laminitis. Ketoprofen is also prescribed to reduce or control fevers due to viral or bacterial infections. Advantages claimed for the use of ketoprofen in horses include inhibition of bradykinin and inhibition of both COX and LOX pathways. This anti-LOX effect is seen in laboratory studies, but has not been demonstrated in actual studies in live horses. It is readily and rapidly absorbed by the intramuscular route and is almost totally bound to plasma albumin in the horse. It is widely distributed in tissues, including the eye and synovial fluid. A cartilage-protective effect that has been seen in cartilage cultures in the laboratory has also not been demonstrated in live horses. It is recommended for musculoskeletal injuries, where a single dose gives good pain relief and anti-inflammatory activity for 24 hours. Ketoprofen is available as 100 mg/ml solution for intravenous injection at a dose of 2.2 mg/kg once daily for up to 5 days.

Adverse effects:
Ketoprofen does not appear to be substantially different from flunixin meglumine for clinical use in horses, but appears to be less likely to cause gastrointestinal ulcers than other NSAIDs. Ketoprofen possesses a wide therapeutic index: injections of 25 times the therapeutic dose are needed to produce acute toxicity. Trials have indicated that Ketoprofen has a wider safety margin, and lower toxicity potential, than both phenylbutazone and flunixin meglumine in the horse..

Withdrawal:
Ketoprofen is eliminated by the kidneys, and can be measured in urine for 2-3 days after a single dose. NCHA does not consider the finding of ketoprofen in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 0.25 µg/ml. When ketoprofen is administered the dose should be accurately calculated according to the actual weight of the horse at 1.0 mg/lb. Each 24 hours, not more than 1.0 gram should be administered which equals 10 ml. of the injectable solution (100mg per milliliter). No part of a dose should be administered during the 6 hours prior to competing.

Diclofenac Sodium (Surpass®)

Pharmacology:
Diclofenac is a non-steroidal anti-inflammatory drug of the phenylacetic acid class. Diclofenac sodium uses a new technology called liposome delivery as a means of carrying the drug past the skin to the targeted tissue. This locally-enhanced topical delivery not only maximizes the penetration of the drug, but purportedly sustains the drug's release in the target tissue. Diclofenac is a non-specific inhibitor of cyclooxygenase (includes both COX-1 and COX-2). It may also have some inhibitory effects on lipooxygenase. By inhibiting COX-2 enzymes, diclofenac reduces the production of prostaglandins associated with pain, hyperpyrexia and inflammation.

Uses/indications:
The equine topical anti-inflammatory cream (Surpass®) is labeled for the control of pain and inflammation associated with osteoarthritis in tarsal, carpal metacarpophalangeal, metarsophalangeal, and proximal (hock, knee, fetlock, pastern) joints for use up to 10 days duration. Surpass is approved for application of a five-inch (5") ribbon of cream twice daily over the affected joint. The craem is rubbed thoroughly into the hair covering the joint until the craem disappears.

Adverse effects:
The topical cream in horses appears to well tolerated. Adverse reactions during the safety study included a gastric ulcer in one horse that received 5.6X the recommended dosage, diarrhea and uterine discharge in one horse that received 2.8X the recommended dosage, and weight loss in four of the six horses in the 5.6X dosage group.

Withdrawal:
Diclofenac is eliminated by the kidneys, and can be measured in urine for 3 days after a single topical administration. NCHA does not consider the finding of diclofenac in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 0.005 μg/ml. Every 12 hours, not more than 73 mg of diclofenac liposomal cream should be administered (not more than 146 mg per 24-hour period) to one affected site. This 73 mg dose equals a 5-inch ribbon of cream not greater than half-an-inch in width, which should be rubbed thoroughly into the hair over the joint or affected site using gloved hands. Do not apply diclofenac cream in combination with any other topical preparations including DMSO, nitrofurazone or liniments, and do not use on an open wound. Diclofenac cream should not be administered for more than 10 consecutive days. Administration of diclofenac cream should be discontinued 6 hours prior to competing.

Firocoxib (Equioxx®)

Pharmacology:
Firocoxib is a recently FDA approved coxib-class NSAID. It is marketed as a selective inhibition of COX-2 (or COX-1 sparing), which inhibit the production of the prostaglandins responsible for pain and inflammatory.

Uses/indications:
Equioxx Oral Paste is indicated in horses for the control of pain and inflammation associated with osteoarthritis. Like most NSAIDs, firocoxib can be useful for treatment of fever, pain, and inflammation associated with other conditions, post-surgery, trauma etc. The recommended dosage of Equioxx for oral administration in horses is 0.045 mg/lb (0.1 mg/kg) of body weight once daily for up to14 days. Each marking on the syringe will treat 250 pounds of body weight, and each notch corresponds to approximately a 50 lb weight increment. To deliver the correct dose, round the horse's body weight up to the nearest 50 pound increment. Slide the knurled ring along the plunger shaft so that the side nearest the barrel is at the appropriate 50 lb weight notch. Rotate the plunger ring 1/4 turn to lock it in place and ensure it is locked.

Adverse effects:

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

Withdrawal:
Firocoxib is eliminated by the kidneys, and can be measured in urine for more than 5 days after a single dose and for up to 20 days after administration for 14 days. NCHA does not consider the finding of firocoxib in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 0.4 μg/ml. When firocoxib is administered the dose should be accurately calculated according to the actual weight of the horse at 0.1 mg/kg. Each 24 hours, not more than 45.5 mg should be administered. No part of a dose should be administered during the 6 hours prior to competing.

Meclofenamic Acid (Arquel®)

Pharmacology:
Meclofenamic acid is a non-steroidal anti-inflammatory drug of the fenamate class. Meclofenamic acid is a very palatable oral granule used in horses for the treatment of inflammatory musculoskeletal conditions. This drug has not been extensively researched in veterinary medicine. Feeding prior to dosing may delay absorption of meclofenamic acid from the horse's stomach.

Uses/indications:
Meclofenamic acid is dosed in horses at 2.2 mg/kg of body weight given as a 20 grams of Arquel® granules to a 1000 lb horse once a day in the feed. It is an unusual NSAID in that its anti-inflammatory and analgesic action can take 36-96 hours to develop. Clinical efficacy can be seen for days once therapy is discontinued. Repeated daily dosing does not result in drug accumulation, therefore this is a useful drug for chronic inflammatory conditions such as navicular disease or bone spavin. Many horses can be maintained comfortably with twice weekly dosing without side effects. In clinical studies, researchers found clinical improvement in the lameness of 2/3 of treated horses.

Adverse effects:
At normal doses, some decrease in blood protein concentrations may be seen. Doses of 68 times the label dose result in toxicity, including mouth ulcers, loss of appetite, depression, edema and weight loss. When administered at the label dose chronically to stallions and pregnant mares, no toxic effects were seen.

Withdrawal:
Meclofenamic acid is eliminated by the kidneys, and can be measured in urine for 96 hours after a single dose. NCHA does not consider the finding of meclofenamic acid in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 2.5 μg/ml. When meclofenamic acid is administered, the dose should be accurately calculated according to the actual weight of the horse. Each 6 hours, not more than 0.5 milligram per pound of body weight should be administered, preferably less. For a 1,000-pound horse, the maximum 12-hour dose is 0.5 gram, which equals one 500-milligram packet of granules. No part of a dose should be administered during the 6 hours prior to competing.

Naproxen (Equiproxen®)

Pharmacology:
Naproxen is a non-steroidal anti-inflammatory drug of the propionic acid derivative. Like other NSAIDs, naproxen can be useful for treatment of fever, pain, and inflammation associated with other conditions, post-surgery, trauma, etc. Equiproxen is indicated in horses for the control of pain and inflammation associated with osteoarthritis. In some cases, it is not as effective in treating joint injuries. Naproxen is absorbed promptly, but full clinical response may not occur for several days. In the horse, Naproxen has been reported to be 50% bioavailability after oral dosing and a half-life of approximately 4 hours.

Uses/indications:
Naproxen is used to treat lameness, musculoskeletal pain from soft tissue injury, muscle soreness, and bone and joint problems. It may take 5-7 days to see a benefitual response after starting treatment. For oral maintenance therapy following initial intravenous dosage, administer 10 mg/kg of body weight twice daily as top dressing in the horse's feed for up to 14 consecutive days. The initial intravenous dosage is 5 mg/kg of body weight. For oral dosage only, administer 10 mg/kg twice daily as a top dressing in the horse's feed for up to 14 consecutive days.

Adverse effects:
Adverse reactions are uncommon in horses. Gastrointestinal problems, such as ulcers, diarrhea, and GI pain may occur in some horses. Rare side effects include kidney damage, bleeding disorders, and protein loss. Naproxen should not be combined with other anti-inflammatory drugs that tend to cause GI ulcers, such as corticosteroids and other NSAIDs.

Withdrawal:
Naproxen is eliminated by the kidneys, and can be measured in urine for 120 hours after a single dose. NCHA does not consider the finding of naproxen in urine a violation. The corresponding plasma sample is analyzed by LC-MS and is a violation when the plasma concentration is in excess of 10 μg/ml. When naproxen is administered, the dose should be accurately calculated according to the actual weight of the horse. Each 24 hours, not more than 4.0 grams per pound of body weight (which equals eight 500-milligram tablets) should be administered. No part of a dose should be administered during the 6 hours prior to competing.

Other Permitted Medications:

- Omeprazole (Gastroguard®)
- Methocarbamol (Robaxin®)
- Furosemide (Lasix®)
- Altrenogest (Regu-mate®)
- Acetazolamide
- Isoxsuprine Hydrochloride
- Dexamethasone
- Ventipulmin ® Syrup
- Acepromazine Maleate* (Medication Report Must be Submitted)

Omeprazole (GastroGard/UlcerGard®)

Pharmacology:

Omeprazole is a gastric acid pump inhibitor that regulates the final step in hydrogen ion production and blocks gastric acid secretion regardless of the stimulus. Omeprazole irreversibly binds to the gastric parietal cell's H+, K+ ATPase enzyme which pumps hydrogen ions into the lumen of the stomach in exchange for potassium ions. Since omeprazole accumulates in the cell cannaliculi and is irreversibly bound to the effect site, the plasma concentration at steady state is not directly related to the amount that is bound to the enzyme. The relationship between omeprazole action and plasma concentration is a function of the rate-limiting process of H+, K+ ATPase activity/turnover. Once all of the enzyme becomes bound, acid secretion resumes only after new H+, K+ ATPase is synthesized in the parietal cell (i.e., the rate of new enzyme synthesis exceeds the rate of inhibition).

Uses/indications:
For the treatment of gastric/stomach ulcers in horses and foals 4 weeks of age and older. Omeprazole is mainly used to prevent ulcers in horses that are subjected to stress or other conditions that make them prone to stomach ulcers. It is also used to treat cases of existing ulcers. Omeprazole is sometimes prescribed as a precaution when NSAIDs, corticosteroids, and other drugs known to cause stomach ulcers are administered. Maximum suppression of acid production occurs three to five days after beginning treatment. For treatment of gastric ulcers, each weight marking on the syringe plunger will deliver sufficient omeprazole to treat 250 lb (114 kg) body weight. For prevention of recurrence of gastric ulcers, each weight marking will deliver sufficient omeprazole to dose 500 lb (227 kg) body weight.

Adverse effects:
In efficacy trials, when the drug was administered at 4 mg/kg omeprazole daily for 28 days and 2 mg/kg omeprazole daily for 30 additional days, no adverse reactions were observed.

Withdrawal:
Omeprazole is eliminated by the kidneys, and can be measured in urine for 48 hours after a single dose. For a 1,000-pound horse, the maximum 24-hour dose is 1.62 grams, which equals a 1000 lb (456 kg) dose marked on the syringe plunger. No part of a dose should be administered during the 6 hours prior to competing.

Methocarbamol (Robaxin®)

Pharmacology:
Methocarbamol's exact mechanism of causing skeletal muscle relaxation is unknown. It is thought to work centrally, perhaps by general depressant effects. It has no direct relaxant effects on striated muscle, nerve fibers, or the motor endplate. It will not directly relax contracted skeletal muscles. The drug has a secondary sedative effect.

Uses/indications:
Intravenous use is indicated as adjunctive therapy of acute inflammatory and traumatic conditions of the skeletal muscle to reduce muscular spasms, and effect striated muscle relaxation.

Adverse effects:
Side effects can include sedation, salivation, emesis, lethargy, weakness and ataxia in dogs and cats. Sedation and ataxia are possible in horses. Because of its CNS depressant effects, methocarbamol may impair the abilities of working horses.

Withdrawal:
Methocarbamol is eliminated by the kidneys, and can be measured in urine for 2 days after a single IV dose. Whenever methocarbamol is administered, the dose should be accurately calculated according to the actual weight of the horse. Each 12 hours, not more than 5.0 mg per pound of body weight should be administered. For a 1000 pound animal, the maximum dose each 12 hours is 5.0 grams, which equals ten 500 milligram tablets or 50 cc of the injectable (100 milligrams per milliliter). No dose should be administered during the 12 hours immediately following the prior dose. No part of a dose should be administered during the 6 hours prior to competing.
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Furosemide (Salix®)

Pharmacology:
Furosemide is a diuretic used in horses to increase urine production and decrease the amount of fluid in tissues and organs. It relieves fluid retention and excessive swelling, and, when used with race horses, it is thought to prevent or diminish the severity of exercise-induced pulmonary hemorrhage.

Uses/indications:
Furosemide is also used in horses for pulmonary edema, congestive heart failure (in combination with other drugs), and allergic reactions. Despite the fact it increases circulation to the kidneys, it does not help kidney function, and is not recommended for kidney disease. The usual parenteral dosage of furosemide in horses is approximately 0.5 mg/lb body weight (1.0 mg/kg).

Adverse effects:
Side effects include dehydration and loss of electrolytes. In some species, furosemide may negatively impact hearing and balance. Excessive use of furosemide will most likely lead to a metabolic alkalosis due to hypochloremia and hypokalemia. The drug should therefore not be used in horses that are dehydrated or experiencing kidney failure. It should be used with caution in horses with liver problems or electrolyte abnormalities. Overdose may lead to dehydration, change in drinking patterns and urination, seizures, GI problems, kidney damage, lethargy, collapse, and coma.

Withdrawal:
Furosemide is eliminated by the kidneys, and can be measured in urine for two days after a single dose. For a 1000-pound horse the maximum daily dose of furosemide in horses is 500 milligrams, which equals 0.5 mg/lb (5 milliliters of the injectable solution) . Furosimide is administered intravenously and no part of the dose should be administered **4** hours prior to competing.

Altrenogest (Regu-Mate®)

Pharmacology:
Altrenogest is an orally administered synthetic progestational agent. It has a chemical name of 17 - hydroxyestra-4,9,11-trien-3-one. Regu-Mate (altrenogest) Solution 0.22% produces a progestational effect in mares. Altrenogest is used for suppression of estrus. The mare will experience a predictable occurrence of estrus following drug withdrawal. This allows a regular cycle during the transition from winter anestrus to the physiological breeding season in mares with active ovaries. By managing the reproductive cycle, horse owners have more control over breeding procedures and the timing of the

arrival of foals.

Uses/indications:
Altrenogest is indicated to suppress estrus in mares to allow a more predictable occurrence of estrus following withdrawal of the drug. It is used clinically to assist mares to establish normal cycles during the transitional period from anoestrus to the normal breeding season often in conjunction with an artificial photoperiod. Draw out appropriate volume of Regu-Mate® solution. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Detach syringe and administer solution orally at the rate of 1mL per 110 pounds body weight (0.044 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare's tongue or on the mare's usual grain ration.

Adverse effects:
Adverse effects of altrenogest appear to be minimal when used at labeled dosages. Occasionally, slight changes in Ca++, K+, alkaline phosphatase and AST were noted in the treatment group, but values were only slightly elevated and only noted sporadically. No pattern or definite changes could be attributed to altrenogest. No outward adverse effects were noted in the treatment group during the trial.

Withdrawal:
Altrenogest is eliminated by the kidneys, and can be measured in urine for 72 hours after a single dose. The use of altrenogest is currently permitted for mares with estrus-related behavioural problems because altrenogest suppresses behavioural estrus in the mare within the 2-3 days following the beginning of the dosing schedule an, at the recommended dose, has no effect on dominance, body mass and condition score. No part of a dose should be administered during the 6 hours prior to competing.

Acetazolamide

Pharmacology:
Acetazolamide is a carbonic anhydrase inhibitor that is used to treat glaucoma, epileptic seizures, Idiopathic intracranial hypertension (pseudotumor cerebri), cystinuria, and dural ectasia. Acetazolamide is available as a generic drug and has been found to be more effective than hydrochlorothiazide in controlling clinical signs of hyperkalemic periodic paralysis. This condition causes attacks of muscle weakness, stiffness, and, sometimes, muscle pain and irregular heartbeat in horses.

Uses/indications:
Acetazolamide is used as an adjunctive treatment for controlling clinical signs of hyperkalemic periodic paralysis (HYPP).

Adverse effects:
Acetazolamide may cause fatigue, drowsiness, fever, pain at injection site, gastrointestinal disturbances, blood dyscrasias, abnormal liver function, electrolyte imbalances, ataxia, convulsions, hearing disturbances, and myopia. Long term therapy may cause renal failure and increased risk of nephrolithiasis.

Withdrawal:
May only be administered to horses documented through DNA testing to be positive (N/H or H/H) for HYPP. While these rules do not contain a maximum allowable plasma concentration level for Acetazolamide, laboratory detection of levels of Acetazolamide that are not consistent

with administration in accordance with the Guidelines may result in prosecution of a rule violation. When acetazolamide is administered, the dose should be accurately calculated according to the actual weight of the horse. Each 24 hours, not more than 3 milligrams per pound of body weight should be administered. For a 1,000-pound horse, the maximum daily dose is 3 grams. No part of a dose should be administered during the 6 hours prior to competing.

Isoxsuprine Hydrochloride (Vasodilan®)

Pharmacology:
Isoxsuprine is a synthetic chemical with epinephrine-Like effects. Its action relates specifically to the walls of arteries which are located in the muscles, internal organs, and extremities. Isoxsuprine causes these arteries to dilate. Isoxsuprine is most commonly used to treat hoof-related problems in the horse, most commonly for laminitis and navicular disease, as its effects as a vasodilator are thought to increase circulation within the hoof to help counteract the problems associated with these conditions.

Uses/indications:
Isoxsuprine has been used in the treatment of navicular disease and laminitis, where it is presumed that the disease is associated with some degree of decreased blood supply. Isoxsuprine also has been used to relax the uterus during the treatment of uterine infections. In other species, it has been suggested that isoxsuprine can be used to attempt to treat premature labor.

Adverse effects:
Isoxsuprine may increase the animal's heart rate, cause changes in blood pressure, and irritate the GI tract. It should therefore be used with caution if combined with other drugs that affect blood pressure, such as sedatives and anesthetic drugs. Because it is a vasodilator, it should not be used in horses that are bleeding, or in mares following foaling.

Withdrawal:
Isoxsuprine is eliminated by the kidneys, and can be measured in urine for 96 hours after a single dose. Each 24 hours, not more than 1.6 milligrams per pound of body weight should be administered (usually divided in two equal doses given 12 hours apart). For a 1,000-pound horse, the maximum daily dose is 1,600 milligrams, which equals 80 20-mg tablets. No part of a dose should be administered during the 6 hours prior to competing.

Dexamethasone Sodium Phosphate (Dexject SP®)

Pharmacology:
Anti-inflammatory and immunosuppressive effects are approximately 30 times more potent than those of corticol (hydrocortisone). Anti-inflammatory effects are complex, but primarily by inhibition of inflammatory cells and suppression of expression of inflammatory mediators (e.g., prostaglandins) Used in treatment of inflammatory and immune-mediated disease.

Uses/indications:
Dexamethasone is widely used as an anti-inflammatory agent. Dosage schedules are based on desired effect. Dexamethasone sodium phosphate is a salt of dexamethasone that is particularly suitable for

intravenous administration because it is highly water soluble, permitting administration of relatively large doses in a small volume of diluent.

Adverse effects:
Use of corticosteroids, depending on the dose, duration and specific steroid, may result in inhibition of endogenous steroid production following drug withdrawal. In patients presently receiving or recently withdrawn from systemic corticosteroid treatments, therapy with a rapidly acting corticosteroid should be considered in unusually stressful situations. Anti-inflammatory corticosteroids, such as dexamethasone, are known to exert a wide range of side-effects. Whilst single high doses are generally well tolerated, they may induce severe side-effects in long term use and when esters possessing a long duration of action are administered. Dosage in medium to long term use should therefore generally be kept to the minimum necessary to control clinical signs. Steroids themselves, during treatment, may cause Cushingoid symptoms involving significant alteration of fat, carbohydrate, protein and mineral metabolism, e.g. redistribution of body fat, muscle weakness and wastage and osteoporosis may result. During therapy effective doses suppress the hypothalamo-pituitreal-adrenal axis.

Gastro-intestinal ulceration has been reported in animals treated with corticosteroids and may be exacerbated by steroids in patients given non-steroidal anti-inflammatory drugs. Steroids may cause enlargement of the liver (hepatomegaly) with increased serum hepatic enzymes. Care should be taken when the product is used for the treatment of laminitis in horses, where there is the possibility that such treatment could worsen the condition. The use of the product in horses for other conditions could induce laminitis and careful observations during the treatment period should be made.

Withdrawal:
Dexamethasone is eliminated by the kidneys, and can be measured in urine for 48 hours after a single dose. The following treatment options are considered therapeutic and are permitted:

a. **Alternative No 1** (2.0 mg or less per 100 pounds IV or IM at **12** or more hours before competition) - Each 24 hours, not more than 2.0 milligrams of dexamethasone injectable solution per 100 pounds of body weight should be administered intravenously or intramuscularly, preferably less. For a 1,000-pound horse, the maximum daily intravenous or intramuscular dose of dexamethasone injectable solution is 20.0 milligrams, which equals 5.0 milliliters of the injectable solution (4.0 milligrams per milliliter). No part of this dose should be administered during the **12** hours prior to competing. Dexamethasone should not be administered for more than five consecutive days.
b. **Alternative No. 2** (1.0 mg or less per 100 pounds IV at **6** or more hours before competition) -- Each 24 hours, not more than 1.0 milligram of dexamethasone injectable solution per 100 pounds of body weight should be administered intravenously, preferably less. For a 1,000-pound horse, the maximum daily intravenous dose of dexamethasone injectable solution is 10.0 milligrams, which equals 2.5 milliliters of the injectable solution (4.0 milligrams per milliliter). No part of this dose should be administered during the **6** hours prior to competing. Dexamethasone should not be administered for more than five consecutive days.

c. **Alternative No. 3** (1.0 mg or less per 100 pounds orally at **6** or more hours before competition) -- Each 24 hours, not more than 1.0 milligram of dexamethasone powder per 100 pounds of body weight should be administered orally, preferably less. For a 1,000-pound horse, the maximum daily oral dose of dexamethasone powder is 10.0 milligrams, which equals one packet of dexamethasone powder (10.0 milligrams per packet). No part of this dose should be administered during the **6** hours prior to competing. Any medicated feed should be either consumed or removed at least six hours prior to competing. Dexamethasone should not be administered for more than five consecutive days.

No part of a dose should be administered during the 6 hours prior to competing.

Ventipulmin ® Syrup

Pharmacology:
Clenbuterol (4-amino-alpha – 3, 5- dichlorobenzyl alcohol hydrochloride) is a beta-2-adrenergic agoinist which provides bronchodilating properties as well as other effects, with minimum effects on the cardiovascular system.

Uses/indications:
Ventipulmin Syrup is indicated for the management of horses affected with airway obstruction, such as occurs in chronic obstructive pulmonary disease (COPD).

Adverse effects:
Ventipulmin Syrup antagonizes the effects of prostaglandin F2 alpha and oxytocin. It should not be used in pregnant mares near term. Because tachycardia may occur, Ventipulmin Syrup should not be used in horses suspected of having cardiovascular impairment. May cause elevated creatine kinase serum levels.

Withdrawal:
Each 12 hours, .5 mg (1/2 cc) or less per 100 pounds may be administered orally. No part of a dose should be administered during the **6** hours prior to competing.

Acepromazine Maleate (PromAce®)

Pharmacology:
Phenothiazine tranquilizer: Inhibits central dopaminergic receptors to cause sedation and tranquilization. Acepromazine also has antimuscarinic action and blocks norepinephrine at adrenergic receptors (e.g., alpha-receptors). Acepromazine is used as a sedative and tranquilizer, as well as a preanesthetic and an anesthetic adjunct.

Uses/indications:
Approved for uses in horses, doses can be administered by PO, IV or IM routes. Clinical signs from acepromazine administration are most prominent during the 3-4 hours after administration, but they may

persist for 7 hours. As a preanesthetic agent, acepromazine has the advantage of producing a tranquilizing effect (e.g., help control behavior) without substantial reduction of alertness and coordination.

Adverse effects:
Acepromazine's effects on blood pressure (hypotension) is well described and an important consideration in therapy. This effect is thought to be mediated by both central mechanisms and through the alpha-adrenergic actions of the drug. In male horses, acepromazine may cause protrusion of the penis, this effect may last 2 hours. Stallions should be given acepromazine with caution as injury to the penis can occur with resultant swelling and permanent paralysis of the retractor muscle.

Withdrawal:
Acepromazine is metabolized by the liver with both conjugated and unconjugated metabolites eliminated by the kidneys, and can be measured in urine for as long as 7 days after a single dose. Each 24 hours, .5 mg or less per 100 pounds may be administered IV, IM, or Oral. Maximum single dose should not exceed 5 mg total which is .5ml of the 10mg/ml injectable solution. A ***written medication report must be submitted*** to show management. No part of a dose should be administered during the **1** hour prior to competing.

Notes:

* Whenever medication is administered, the dose should be accurately calculated according to the actual weight of the horse.

** Any medicated feed must be consumed and/or removed at least 6 hours prior to competing.

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