Think Before You Reach for an NSAID for Your Horse

Why You Should Consider Reaching Out to Your Veterinarian Before Reaching for an NSAID.

Equine lameness seems to happen at the most inopportune times, and it's one of the main reasons for removing a horse from athletic activity. When lameness appears, horse owners are often quick to reach for a non-steroidal anti-inflammatory drug (NSAID). In fact, a survey found 82 percent of horse owners use NSAIDs without consulting their veterinarian.[1] But that may not be the smart move.

"It's important for horse owners to consult their veterinarian before giving an NSAID," says Hoyt Cheramie, DVM, MS, Senior Manager, Merial Large Animal Veterinary Services. "The best option – and the shortest path back to soundness – may be a medication, treatment or protocol the horse owner hasn't considered."

"In addition, no medication is without risks," says Cheramie. "Your veterinarian is the best person to help you monitor your horse's health for potential side effects or lack of efficacy. Keeping your veterinarian involved, even if it's just informing them of your treatment decision, will provide them with important information in the future if the issue comes up again."

Your equine veterinarian considers many factors before prescribing any treatment, including an NSAID:

- What is the horse's history?
- Is the diagnosis a simple lameness or could it be something else?
- What treatment options are available?
- What is the horse owner's budget and resources?

If your veterinarian does recommend an NSAID, they'll take into consideration:

- Has this horse been given this medication before?
- What dosage should the horse receive, and what is the best route of administration?
- What are the potential side effects of the treatment or medication?

The decision-making process can be complex, which is why most equine NSAIDs are available only with a prescription. If for some reason your horse does have a reaction or fails to improve, ensuring your veterinarian is fully aware of the situation will be a benefit.

Based on your horse's exam, your veterinarian may suggest EQUIOXX® (firocoxib) to treat pain and inflammation associated with osteoarthritis. EQUIOXX is the first and only coxib NSAID approved for horses and is available in three formulations. EQIUOXX Injection, Oral Paste and Tablets provide a choice to fit you and your horse's needs.

Regardless of discipline, from pleasure riding to top-level jumping, when your horse is lame, it can impact not only your short-term competitive goals but also your horse's long-term health. So, before you reach for that old tube or bottle, talk to your veterinarian about

all of your options to help effectively manage lameness, pain and inflammation in your horse.

IMPORTANT SAFETY INFORMATION
As with any prescription medication, prior to use, a veterinarian should perform a physical examination and review the horse's medical history. A veterinarian should advise horse owners to observe for signs of potential drug toxicity. As a class, nonsteroidal anti-inflammatory drugs may be associated with gastrointestinal, hepatic and renal toxicity. Use with other NSAIDs, corticosteroids or nephrotoxic medication should be avoided. EQUIOXX has not been tested in horses less than 1 year of age or in breeding horses, or pregnant or lactating mares. For additional information, please refer to the prescribing information or visit www.equioxx.com.

About Boehringer Ingelheim Animal Health
On January 1st, 2017, Merial became part of the Boehringer Ingelheim group. As the second largest animal health business in the world, Boehringer Ingelheim is committed to making the industry even better at improving animal health. With more than 10,000 employees worldwide, Boehringer Ingelheim Animal Health has products available in more than 150 markets and a global presence in 99 countries. For more information about Boehringer Ingelheim Animal Health, click here.

About Boehringer Ingelheim
Boehringer Ingelheim is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, Boehringer Ingelheim operates presently with a total of some 50,000 employees worldwide. The focus of the family-owned company, founded in 1885, is on researching, developing, manufacturing and marketing new medications of high therapeutic value for human and veterinary medicine. In 2015, Boehringer Ingelheim achieved net sales of about 14.8 billion euros. R&D expenditure corresponds to 20.3 per cent of net sales. For more information, please visit www.boehringer-ingelheim.com.

[1]Andrews F, McConnico R. Cause for concern: Evidence that therapeutic dosing of nonselective NSAIDs contributes to gastrointestinal injury. *Equine Vet Education.* 2009;21(12):663-664.

Equioxx®
(firocoxib)

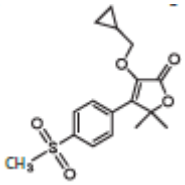
Non-steroidal anti-inflammatory drug

Oral Paste/Tablets
For oral use in horses only

Injection
For intravenous use in horses only

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:



EQUIOXX (firocoxib) belongs to the coxib class of non-narcotic, non-steroidal anti-inflammatory drugs (NSAID). Firocoxib is a white crystalline compound described chemically as 3-(cyclopropylmethoxy)-4-(4-(methylsulfonyl)phenyl)-5, 5-dimethylfuranone. The empirical formula is $C_{17}H_2O_5S$, and the molecular weight is 336.4 g/mol. The structural formula is shown to the right.
EQUIOXX Injection is a colorless to pale yellow solution. Each mL of EQUIOXX Injection contains 20mg of firocoxib as a free base, 550 mg of polyethylene glycol (PEG 400) and 600 mg of glycerol formal.

Indications:

EQUIOXX is indicated for the control of pain and inflammation associated with osteoarthritis in horses.

Dosage and Administration:

Always provide the Client Information Sheet with the prescription. The recommended dosage of EQUIOXX Injection for intravenous administration in horses is 0.04mg/lb (0.09 mg/kg) of body weight once daily for up to 5 days. EQUIOXX Injection is a non-aqueous solution and should not be mixed with aqueous solutions (Do not flush through intravenous lines using aqueous flush solutions).
If further treatment is needed, EQUIOXX Oral Paste or EQUIOXX Tablets can be used at a dosage of 0.045 mg/lb (0.1 mg/kg) body weight for up to an additional 9 days of treatment.
The recommended dosage of EQUIOXX Oral Paste is 0.045 mg/lb (0.1 mg/kg) of body weight once daily for up to 14 days. In target animal safety studies, toxicity was seen at the recommended dose when the duration of treatment exceeded 30 days. Each marking on the syringe will treat 250 lbs 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 lb increment (if the body weight is an exact 50 lb increment, do not round up).

1) While holding plunger, turn the knurled ring on the plunger ¼ turn to the left and slide the knurled ring along the plunger shaft so that the side nearest the barrel is at the appropriate 50 lb weight notch, aligning the arrow on the plunger with the notch on the ring, as shown in the pictogram.
2) Lock the ring in place by making ¼ turn to the right. Ensure it is locked (it should no longer slide)

The recommended dosage of EQUIOXX Tablets is one 57mg tablet, for oral administration in horses weighing 800-1300lbs, once daily for up to 14 days.

The overall duration of treatment with any firocoxib formulation in horses, including EQUIOXX Injection, Oral Paste or Tablets will be dependent on the response observed, but should not exceed 14 days. EQUIOXX may be given with or without food.

Contraindications:

Horses with hypersensitivity to firocoxib should not receive EQUIOXX.

Warnings:

EQUIOXX Tablets and Paste are for oral use in horses only. EQUIOXX Injection is for intravenous use in horses only. Do not use in horses intended for human consumption.
Keep EQUIOXX Tablets out of the reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

Human Warnings:

Not for use in humans. Keep this and all medications out of the reach of children. Consult a physician in case of accidental human exposure or ingestion.

Precautions:

Horses should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests should be conducted to establish hematological and serum biochemical baseline data before and periodically during administration of any NSAID. Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription. See Information for Owner or Person Treating Horse section of this package insert.
Treatment with EQUIOXX should be terminated if signs such as inappetance, colic, abnormal feces, or lethargy are observed. As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Horses that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for adverse events are those that are dehydrated, on diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached or avoided. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin 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 and/or gastrointestinal perforation, concomitant use of EQUIOXX with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. The concomitant use of protein bound drugs with EQUIOXX has not been studied in horses. The influence of concomitant drugs that may inhibit the metabolism of EQUIOXX has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. The safe use of EQUIOXX in horses less than one year of age, horses used for breeding, or in pregnant or lactating mares has not been evaluated. Consider appropriate washout times when switching from one NSAID to another NSAID or corticosteroid.

Adverse Reactions:

The safety and effectiveness of EQUIOXX Tablets was supported by a relative bioavailability study comparing EQUIOXX Tablets to the EQUIOXX Oral Paste (See Clinical Pharmacology section), in addition to pharmacovigilance information, and target animal safety data for existing firocoxib-containing products in horses. The effectiveness of EQUIOXX Injection was established in a biocomparability study demonstrating that EQUIOXX Oral Paste is bioequivalent to EQUIOXX Injection. Thus additional studies were not performed to support the effectiveness of EQUIOXX Injection or Tablets, nor were additional studies conducted to support safety of EQUIOXX Tablets. The safety of EQUIOXX Injection was established through a target animal safety study of EQUIOXX Injection administered IV followed by EQUIOXX Oral Paste (See Animal Safety Section).
In controlled field studies, 127 horses (ages 3 to 37 years) were evaluated for safety when given EQUIOXX Oral Paste at a dose of 0.045 mg/lb (0.1 mg/kg) orally once daily for up to 14 days. The following adverse reactions were observed. Horses may have experienced more than one of the observed adverse reactions during the study.

Table 1: Adverse Reactions Seen in U.S. Field Studies with EQUIOXX Oral Paste

Adverse Reactions	EQUIOXX n = 127	Active Control n = 125
Abdominal pain	0	1
Diarrhea	2	0
Excitation	1	0
Lethargy	0	1
Loose stool	1	0
Polydipsia	0	1
Urticaria	0	1

EQUIOXX Oral Paste was safely used concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics. Therefore based on relative bioavailability of firocoxib across formulations, concomitant use of EQUIOXX Injection or EQUIOXX Tablets with other therapies is expected to have the same safety profile.
The Safety Data Sheet (SDS) contains more detailed occupational safety information. To report suspected adverse events, for technical assistance, or to obtain a copy of the SDS, contact Merial at 1-877-217-3543. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

Information for Owner or Person Treating Horse:

A Client Information Sheet should be provided to the person treating the horse. Treatment administrators and caretakers should be aware of the potential for adverse reactions and the clinical signs associated with NSAID intolerance. Adverse reactions may include erosions and ulcers of the gums, tongue, lips and face, weight loss, colic, diarrhea, or icterus. Serious adverse reactions associated with this drug class can occur without warning and, in some situations, result in death. Clients should be advised to discontinue NSAID therapy and contact their veterinarian immediately if any of these signs of intolerance are observed. The majority of patients with drug-related adverse reactions recover when the signs are recognized, drug administration is stopped, and veterinary care is initiated.

Clinical Pharmacology:

When administered as a 0.045 mg/lb (0.1 mg/kg) dose in oral paste to adult horses with normal access to roughage, feed, and water, the absolute bioavailability of firocoxib from EQUIOXX Oral Paste is approximately 79%. Following oral administration, drug peak concentration (Cmax) of 0.08 mcg/mL can be reached at 4 hours (Tmax) post-dosing. However, in some animals, up to 12 hours may be needed before significant plasma concentrations are observed. Little drug amount distributes into blood cells.
A pharmacokinetic study was conducted to compare the relative bioavailability of an oral firocoxib tablet containing 57 mg firocoxib (EQUIOXX Tablets) to the paste formulation (EQUIOXX Oral Paste). The criteria for the Test/Reference (T/R) ratios and the 90% Confidence Intervals (CI) of EQUIOXX Tablets (test product) were adjusted on the basis of the safety and effectiveness data for EQUIOXX Oral Paste (reference product). The lower bound of the 90% CI for effectiveness was defined by the minimal effective plasma concentration in the study used to support the dosage characterization of EQUIOXX Oral Paste. Effectiveness was based upon the area under the plasma drug concentration-time curve to the last quantifiable concentration (AUClast), with the effectiveness criteria set at a T/R ratio of greater than or equal to 0.77 and a corresponding lower bound for the 90% CI set at 0.71. The upper bound of the 90% CI for safety was defined by the maximum safe plasma concentration (Cmax) in the study used to establish a margin of safety for EQUIOXX Oral Paste. Based upon that margin of safety, product safety was defined as a T/R of less than or equal to 1.53, with a corresponding upper bound for the 90% CI of 1.71.

The relative bioavailability study was a randomized, two period, two sequence crossover study in thirty horses. Each horse received a single tablet (57 mg firocoxib) and a single tube of paste (56.7 mg firocoxib). Blood samples were collected at 15 minutes, 45 minutes, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 32, 48, 72, 96 and 120 hours following each treatment. Samples were analyzed by LC-MS/MS for firocoxib concentrations. The results of the relative bioavailability study are summarized in Table 2. The Cmax and AUClast of EQUIOXX Tablets were within the adjusted 90% CI for safety and effectiveness and met the criteria established for successfully demonstrating that EQUIOXX Tablets will be safe and effective. Therefore, EQUIOXX Tablets and EQUIOXX Oral Paste are acceptable as pharmaceutical alternatives.
There was a substantial difference in the Tmax (time to maximum plasma concentration) between EQUIOXX Oral Paste and EQUIOXX Tablets. The Tmax ranged from 0.25-4 hours for EQUIOXX Oral Paste and 0.25-12 hours for EQUIOXX Tablets. The difference in the rate and extent of absorption was greatest within the first three hours after administration. The mean terminal elimination half-life of EQUIOXX Oral Paste (45.45 hours) was similar to that of EQUIOXX Tablet (44.49 hours).

Table 2: Relative Bioavailability Results for EQUIOXX Oral Paste (Reference) and EQUIOXX Tablets (Test) (n=30 horses)

Parameter	Units	Reference Geometric Mean	Test Geometric Mean	Test/Reference	Lower 90% CI	Upper 90% CI
Cmax	ng/mL	78.44	58.85	0.75	67.92	82.88
AUC last	hr*ng/mL	2515.77	2336.32	0.93	86.37	99.85

Cmax= maximum observed plasma concentration
AUClast= Area Under the Curve to the last quantifiable time point
CI= Confidence Interval

Based on the comparison data between the intravenous and oral administration, the area under the curve (AUC) for both routes of administration was the same. The average AUC ratio of injectable to the oral product was 103%. The average peak plasma concentration observed one minute following firocoxib intravenous administration was approximately 3.7 fold greater than the observed average peak plasma concentration reached after administration of the oral paste (oral Tmax=2.02 hours). The average plasma concentrations following IV injection and oral administration were similar by 2 hours post-dose, after which the concentrations proceeded to decline in parallel. The terminal elimination half-life (T ½ el) values were not significantly different (p>0.05), with values ranging from 14.6 to 68.0 hours (mean=31.5 hours) for the oral paste and from 12.6 to 66.3 (mean=33.0 hours) for the intravenous solution.

The major metabolism mechanism of firocoxib in the horse is decyclopropylmethylation followed by glucuronidation of that metabolite. Based upon radiolabel studies done for the firocoxib paste formulation, the majority of firocoxib is eliminated in the urine as the glucuronide conjugate of decyclopropylmethylated metabolite. Despite a high rate of plasma protein binding (98%), firocoxib exhibits a large volume of distribution (mean Vd(ss) = 1652 mL/kg). The terminal elimination half-life (T1/2) in plasma averages 30-40 hours after IV, oral paste or tablet dosing. Therefore, drug accumulation occurs with repeated dose administrations and steady state concentrations are achieved beyond 6-8 daily oral doses in the horse. Dose linearity exists from 1X-2X of 0.1mg/kg/day after oral administration. Steady-state plasma firocoxib concentrations at 4 and 24 hours post administration were the same following intravenous or oral administration at each dose in the range of 1X to 5X.

Mode of Action:

Firocoxib is a cyclooxygenase-inhibiting (coxib) class, non-narcotic, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic activity[1] in animal models. Based on *in vitro* horse data, firocoxib is a selective inhibitor of prostaglandin biosynthesis through inhibition of the inducible cyclooxygenase-2-isoenzyme (COX-2)[2,3]. Firocoxib selectivity for the constitutive isoenzyme, cyclooxygenase-1 (COX-1), is relatively low. However, the clinical significance of these *in vitro* selectivity findings has not been established.

Effectiveness:

Two hundred fifty-three client-owned horses of various breeds, ranging in age from 2 to 37 years and weighing from 595 to 1638 lbs, were randomly administered EQUIOXX Oral Paste or an active control drug in multi-center field studies. Two hundred forty horses were evaluated for effectiveness and 252 horses were evaluated for safety. Horses were assessed for lameness, pain on manipulation, range of motion, joint swelling, and overall clinical improvement in a non-inferiority evaluation of EQUIOXX Oral Paste compared to an active control. At study's end, 84.4% of horses treated with EQUIOXX Oral Paste were judged improved on veterinarians' clinical assessment, and 73.8% were also rated improved by owners. Horses treated with EQUIOXX Oral Paste showed improvement in veterinarian-assessed lameness, pain on manipulation, range of motion, and joint swelling that was comparable to the active control.
The effectiveness of EQUIOXX Tablets and EQUIOXX Injection were established in relative bioavailability studies comparing these to EQUIOXX Oral Paste. Therefore additional field studies were not performed to support the effectiveness of EQUIOXX Tablets or EQUIOXX Injection. (See Clinical Pharmacology).

Animal Safety:

In a target animal safety study conducted to support the approval of EQUIOXX Oral Paste, firocoxib was administered orally to healthy adult horses (two male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 30 days. Administration of firocoxib at 0.3 and 0.5 mg/kg body weight was associated with an increased incidence of oral ulcers as compared to the control group but, no oral ulcers were noted with 0.1 mg/kg. There were no other drug-related adverse findings in this study. In another target animal safety study, firocoxib was administered orally to healthy adult horses (four males or male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 42 days. Administration of firocoxib at 0.1, 0.3 and 0.5 mg/kg body weight was associated with delayed healing of pre-existing oral (lip, tongue, gingival) ulcers. In addition, the incidence of oral ulcers was higher in all treated groups as compared to the control group. Clinical chemistry and coagulation abnormalities were seen in several horses in the 0.5 mg/kg (5X) group. One 5X male horse developed a mildly elevated BUN and creatinine over the course of the study, prolonged buccal mucosal bleeding time (BMBT), and a dilated pelvis of the right kidney. Another 5X male had a similar mild increase in creatinine during the study but did not have any gross abnormal findings. One female in the 5X group had a prolonged BMBT, bilateral tubulointerstitial nephropathy and bilateral papillary necrosis. Tubulointerstitial nephropathy occurred in one 3X female, two 3X male horses, and the 5X female horse discussed above with the prolonged BMBT. Papillary necrosis was present in one 1X male horse and the 5X female horse discussed above. Despite the gross and microscopic renal lesions, all of the horses were clinically healthy and had normal hematology, clinical chemistry and urinalysis values.
In another target animal safety study, firocoxib was administered orally to healthy adult horses (three females, two male castrates and one male per group) at 0, 0.25 mg/kg, 0.75 mg/kg and 1.25 mg/kg (2.5, 7.5 and 12.5X the recommended dose of 0.1 mg/kg) for 92 days. An additional group of three females, two male castrates and one male per group, was dosed at 1.25 mg/kg for 92 days but was monitored until Days 147-149. There were treatment-related adverse events in all treated groups. These consisted of ulcers of the lips, gingiva and tongue and erosions of the skin of the mandible and head. Gross and microscopic lesions of the kidneys consistent with tubulointerstitial nephropathy were seen in all treated groups. Papillary necrosis was seen in the 2.5X and 12.5X groups. In addition, several 12.5X horses had elevated liver enzymes (GGT, SDH, AST and ALT). One 2.5X horse had increased urine GGT and urine protein levels which was due to renal hemorrhage and nephropathy. Gastric ulcers of the margo plicatus and glandular area were more prevalent in the 2.5X and 7.5X groups, but not seen in the 12.5X group. The group of horses that were monitored until Days 147-149 showed partial to full recovery from oral and skin ulcers, but no recovery from tubulointerstitial nephropathy.
A target animal safety study was conducted to assess the safety of EQUIOXX Injection followed by EQUIOXX Oral Paste in the horse. Thirty-two clinically healthy adult horses received EQUIOXX Injection intravenously once daily for five days at doses of either 0 mg/kg (control group); 0.09 mg/kg (1X); 0.27 mg/kg (3X); or 0.45 mg/kg (5X the recommended dose). This was followed by once daily oral administration of EQUIOXX Oral Paste for nine days at doses of either 0 mg/kg (control group); 0.1 mg/kg (1X); 0.3 mg/kg (3X); or 0.5 mg/kg (5X the recommended dose). This sequence (five days of EQUIOXX Injection followed by nine days EQUIOXX Paste, for a total of 14 days) was repeated three times for a total treatment duration of 42 days (3X the recommended treatment duration of 14 days).
Two male 5X horses demonstrated a white focus in the renal cortex which correlated with tubulointerstitial nephropathy microscopically. The presence of tubulointerstitial nephropathy was considered treatment-related.
One horse from the control group and two horses from the 5X group had injection site swellings during treatment. Injection site changes characterized by inflammatory cell influx and rarely tissue necrosis were seen in all study groups including the control group.
There was a dose-dependent increase in the incidence of oral ulcers and erosions.
Elevated hepatic enzymes (GGT or AST) were noted in all study groups at one or more timepoints. One male 5X horse with an elevated GGT value on Day 42 was noted to have tubulointerstitial nephropathy at the time of necropsy. For all horses, these hepatic enzyme elevations generally returned to the reference range by the next time point.
Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription. For technical assistance or to report suspected adverse events, call 1-877-217-3543.

Storage Information:

EQUIOXX Injection: Store at 68-77°F (20-25°C) with excursions between 59-86°F (15-30°C) permitted.
EQUIOXX Oral Paste: Store below 86°F (30°C) with brief excursions up to 104°F (40°C) permitted.
EQUIOXX Tablets: Store between 59-86°F (15-30°C) with brief excursions up to°F (40°C) permitted.

How Supplied:

EQUIOXX Injection is supplied in sterile, 25mL amber glass vials for multi-dose use.
NADA 141-313, Approved by FDA.
Made in Germany.

EQUIOXX Oral Paste is available in packs of 20 individually-boxed syringes and packs of 72 individually wrapped syringes. Each syringe contains 6.93g of EQUIOXX paste, sufficient to treat a 1250 lb. horse.
NADA 141-253, Approved by FDA.
Made in Brazil.

EQUIOXX Tablets are available as round, beige to tan, half-scored tablets, containing 57mg firocoxib. EQUIOXX Tablets are supplied in 60 and 180 count bottles.
NADA 141-458, Approved by FDA.
Made in France.

References:

[1] McCann ME, Rickes EL, Hora DF, Cunningham PK et al. *In vitro* effects and *In vivo* efficacy of a novel cyclooxygenase-2 inhibitor in cats with lipopolysaccharide-induced pyrexia. Am J Vet Res. 2005 Jul;66 (7):1278-84

[2] McCann ME, Anderson DR, Brideau C et al. *In vitro* activity and *in vivo* efficacy of a novel COX-2 inhibitor in the horse. Proceedings of the Academy of Veterinary Internal Medicine. 2002. Abstract 114, p.789.

[3] Data on file.

Manufactured for:
Merial, Inc.,1-877-217-3543

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