Equioxx®

Oral Paste for Horses (firocoxib)

Non-steroidal anti-inflammatory drug
Information for Horse Owners

EQUIOXX® Oral Paste is administered for up to 14 days for the control of pain and inflammation associated with osteoarthritis in horses.

This summary contains important information about EQUIOXX. You should read this information before you start giving your horse EQUIOXX paste and review it each time your prescription is refilled. This sheet is provided only as a summary and does not take the place of instructions from your veterinarian. Talk to your veterinarian if you do not understand any of this information or you want to know more about EQUIOXX.

What is EQUIOXX?
EQUIOXX is a veterinary prescription non-steroidal anti-inflammatory drug (NSAID) of the coxib class used to control pain and inflammation associated with osteoarthritis in horses. Osteoarthritis (OA) is a painful condition caused by progressive "wear and tear" of cartilage and other parts of the joints that may result in the following changes or signs in your horse:

- Limping or lameness.
- Decreased activity or exercise (reluctance to stand, walk, trot or run, or difficulty in performing these activities).
- Stiffness or decreased movement of joints.

How to give EQUIOXX to your horse.
EQUIOXX should be given according to your veterinarian's instructions. Do not change the way you give EQUIOXX to your horse without first speaking with your veterinarian. Do not exceed 14 days of treatment.

The recommended dosage of EQUIOXX (firocoxib) for oral administration in horses is 0.045 mg/lb (0.1 mg/kg) of body weight once daily for up to 14 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 (if the body weight is an exact 50 pound increment, do not round up).

EQUIOXX may be given with or without food.

What kind of results can I expect when my horse is on EQUIOXX for OA?
While EQUIOXX is not a cure for osteoarthritis, it can control the pain and inflammation associated with OA and can improve your horse's mobility.

- Response varies from horse to horse, but improvement can be quite dramatic.
- Improvement can be seen in just a few hours in most horses.

Which horses should not receive EQUIOXX?
Your horse should not be given EQUIOXX if he/she:

- Has an allergic reaction to firocoxib, the active ingredient in EQUIOXX.
- Has previously had an allergic reaction (such as hives, facial or lower limb swelling, or red or itchy skin) to aspirin or other NSAIDs.
- Is presently taking aspirin, phenylbutazone, flunixin meglumine, diclofenac, ketoprofen, or other NSAIDs or corticosteroids.
- The safety of EQUIOXX has not been determined in horses less than one year of age or in breeding horses, pregnant or lactating mares.

EQUIOXX paste should only be given orally to horses.

- EQUIOXX is not for use in horses intended for human food consumption.
- People should not take EQUIOXX. Keep EQUIOXX and all medications out of the reach of children. Consult a physician in case of accidental ingestion by humans.

What to tell/ask your veterinarian before giving EQUIOXX.
Talk to your veterinarian about:

- The signs of OA you have observed in your horse, such as limping or stiffness.
- If any tests, such as X-rays, will be done before EQUIOXX is prescribed.
- How often your horse may need to be examined by your veterinarian.
- The risks and benefits of using EQUIOXX.

Tell your veterinarian if your horse has ever had the following medical problems:

- Any side effects from taking EQUIOXX or other NSAIDs, such as aspirin or phenylbutazone.
- Any kidney disease.
- Any liver disease.
- Any gastrointestinal ulcers.

Tell your veterinarian about:

- Other medical problems or allergies that your horse has now, or has had in the past.
- All medicines that you are giving or plan to give to your horse, including those you can get without a prescription and any dietary supplements.

Tell your veterinarian if you plan to breed your horse, or if your mare is pregnant or nursing a foal.

What are the possible side effects that may occur in my horse during EQUIOXX therapy?
EQUIOXX, like other NSAIDS, may cause some side effects. Serious side effects associated with NSAID therapy in horses can occur with or without warning. The most common side effects associated with EQUIOXX therapy involve the tongue, lips and skin of the mouth and face (erosions and ulcers of the mucosa and skin) and the kidney. Gastrointestinal, kidney and liver problems have also been reported with other NSAIDs. Look for the following side effects that may indicate your horse is having a problem with EQUIOXX or may have another medical problem:

- Sores or ulcers on the tongue and inside of mouth.
- Sores, scabs, redness, or rubbing of the facial skin, particularly around the mouth.
- Change in eating or drinking habits (frequency or amount consumed).
- Change in urination habits (frequency or color).
- Yellowing of gums, skin, or whites of the eyes (jaundice).
- Unexpected weight loss.
- Change in behavior (such as increased or decreased activity level).

It is important to stop therapy and contact your veterinarian if you think your horse has a medical problem or side effect while taking EQUIOXX paste. If you have additional questions about possible side effects, talk with your veterinarian or call 1-888-637-4251.

Can EQUIOXX be given with other medications?
EQUIOXX should not be given with other NSAIDs (for example, aspirin, phenylbutazone, diclofenac, ketoprofen or flunixin) or systemic corticosteroids (for example, prednisone, cortisone, dexamethasone, or triamcinolone).
Tell your veterinarian about all medications that you have given your horse in the past, and any medications you are planning to give with EQUIOXX paste. This should include other medicines that you can get without a prescription or any dietary supplements. Your veterinarian may want to check that all of your horse's medicines can be given together.

What do I do in case my horse receives more than the prescribed amount of EQUIOXX?

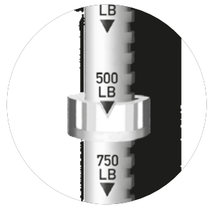
- Consult your veterinarian if your horse receives more than the prescribed amount of EQUIOXX.

What else should I know about EQUIOXX?

- This sheet provides a summary of information about EQUIOXX paste and general information about NSAIDs. If you have any questions or concerns about EQUIOXX or osteoarthritis pain, talk with your veterinarian.
- As with all prescribed medicines, EQUIOXX paste should only be given to the horse for which it is prescribed. It should be given to your horse only for the condition for which it is prescribed, at the labeled dose and duration.
- It is important to periodically discuss your horse's response to EQUIOXX paste. Your veterinarian will determine if your horse is responding as expected and if your horse should continue receiving EQUIOXX paste.

DOSAGE AND ADMINISTRATION:
Always provide the Client Information Sheet with the prescription. The recommended dosage of EQUIOXX (firocoxib) for oral administration in horses 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 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 (if the body weight is an exact 50 pound 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).



Boehringer Ingelheim

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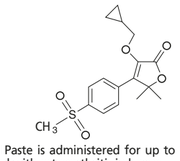
Equioxx®
Oral Paste for Horses (firocoxib)

Non-steroidal anti-inflammatory drug for oral use in horses only.
CAUTION: Federal 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 (NSAIDs). Firocoxib is a white crystalline compound described chemically as 3-(cyclopropylmethoxy)-4-(4-(methylsulfonyl)phenyl)-5,5-dimethylfuranone. The empirical formula is $C_{17}H_{20}O_5S$, and the molecular weight is 336.4. The structural formula is shown below:



Indications: EQUIOXX Oral Paste is administered for up to 14 days 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 (firocoxib) for oral administration in horses 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 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 (if the body weight is an exact 50 pound increment, do not round up).
EQUIOXX may be given with or without food.

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.
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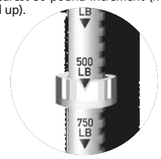

Contraindications: Horses with hypersensitivity to firocoxib should not receive EQUIOXX Oral Paste.
Warnings: For oral use in horses only. Do not use in horses intended for human consumption.
Human Warnings: Not for use in humans. Keep this and all medications out of the reach of children. Consult a physician in case of accidental ingestion by humans.
Animal Safety: 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 1-888-637-4251.
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 Oral Paste with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. The concomitant use of protein bound drugs with EQUIOXX Oral Paste has not been studied in horses. The influence of concomitant drugs that may inhibit the metabolism of EQUIOXX Oral Paste has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. The safe use of EQUIOXX Oral Paste in horses less than one year in 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: 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.

Adverse Reactions Seen in U.S. Field Studies
EQUIOXX (firocoxib) Oral Paste was safely used concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics, during the field studies. The safety data sheet (SDS) contains more detailed occupational safety information.
To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or online at www.fda.gov/reportanimalae.

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

Information for Owner or Person Treating Horse: You should give a Client Information Sheet to the person treating the horse and advise them 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 Pharmacokinetics / Pharmacodynamics:
Pharmacokinetics: 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 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. The major metabolism mechanism of firocoxib in the horse is decyclopropylmethylation followed by glucuronidation of that metabolite. Based upon radiolabel studies, the majority of firocoxib is eliminated in the urine as the 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 ($T^1/2$) in plasma averages 30-40 hours after IV or oral paste 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 0.1 mg/kg/day.
Mode of action: EQUIOXX (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 date, firocoxib is a selective inhibitor of prostaglandin biosynthesis through inhibition of 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.
Acceptability: EQUIOXX Oral Paste was rated both convenient to administer (95.3%) and acceptable to the horse (97.6%) by owners in the multi-center field study.
Animal Safety: In a target animal safety study, 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.
Storage Information: Store below 86°F (30°C). Brief excursions up to 104°F (40°C) are permitted.
How Supplied: EQUIOXX is available in packs of 20 individually-boxed syringes and packs of 72 individually wrapped syringes. Each syringe contains 6.93 grams of EQUIOXX paste, sufficient to treat a 1250 lb. horse.

[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.

Marketed by: Boehringer Ingelheim Animal Health USA Inc. Duluth, GA 30096
Made in Brazil
Approved by FDA under NADA # 141-253

Rev. 11-2019

Boehringer Ingelheim

200-55h2h7

Code: 147455-002 | **Cancel And Replace: 603003679**

PRODUCT: EQUIOXX SHP LABEL	COUNTRY: USA (US)	DIMENSIONS	mm =169 X 125	inches =N/A	PKG-ES =40033

Colors | Please use the official PANTONE®(P) matching system for an accurate color representation.

P 660	BLACK		
CUT	VARNISH	NO PRINT	

Version A - 26 DEZ 2019 - 14h00 - BI INTEGRATION
B - 06 FEV 2020 - 14h50 - text change

Paulinia
AG

RELEASE:

NOTE FOR THE SUPPLIER: N/A

Marketing approval:

Regulatory approval:

Additional approval: (if applicable)

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