Non-stereoidal anti-inflammatory drug for intraocular 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 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_{26}H_{26}O_{5}S, and the molecular weight is 356.50. The structural formula is shown below:

![Structural Formula of Firocoxib](image)

EQUIOXX Injection is a colorless to pale yellow solution. Each mL of EQUIOXX Injection for Horses contains 20 mg of firocoxib as a free base, 550 mg of polyethylene glycol (PEG 4000) and 600 mg of glycerin solution.

Indications: EQUIOXX Injection is administered for up to 5 days for the control of pain and inflammation associated with osteoarthritis in horses.

Dosage and Administration: Always provide the Client Information Sheet with the prescribed dosage. The recommended dosage of EQUIOXX injection for intravenous administration in horses is 0.04 mg/kg (0.09 mg/kg) of body weight once daily for up to 5 days. If further treatment is needed, EQUIOXX (firocoxib) Oral Paste for horses can be used at a dosage of 0.045 mg/kg (0.1 mg/kg) body weight for an additional 8 days of treatment. The overall duration of treatment with EQUIOXX Injection and EQUIOXX Oral Paste will depend on the response observed, but should not exceed 14 days. See EQUIOXX Oral Paste for horses package insert for dosage and administration. EQUIOXX Injection is not an aqueous solution and should not be mixed with any other solutions (Do not flush through intraocular lines using aqueous flush solutions).

Contraindications: Horses with hyperesthesia to firocoxib should not receive EQUIOXX Injection.

Warnings: For intraocular 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 human exposure.

Animal Safety: Clients should be advised to observe for signs of potential drug toxicity and to give a Client Information Sheet with each prescription.

For technical assistance or to report suspected adverse events, call 1-877-F27-3543.

Precautions: Horses under 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 inappetence, colic, abnormal foaling, or lethargy are observed.

As a class, cyclooxygenase inhibitor 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 debilitated, on diuretic therapy, or those with existing renal, cardiovascular, 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-inflammatory effects result in clinically significant disease in patients with underlying or precipitating disease that has not been previously diagnosed. Since many NSAIDs possess the potential to produce gastrointestinal ulcerations and/or gastrointestinal perforation, concurrent use of EQUIOXX Injection with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided.

The concurrent use of protein bound drugs with EQUIOXX injection for horses has not been studied in horses. The influence of concomitant drugs that may inhibit the metabolism of firocoxib should not have been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

The safe use of EQUIOXX Injection for horses has not been evaluated in horses less than one year of age, horses used for breeding, or in pregnant or lactating mares.

Consider appropriate washout times when switching from one NSAID to another NSAID or corticosteroid.

Adverse Reactions: The effectiveness of EQUIOXX injection was established in a biocomparability study demonstrating that EQUIOXX Oral Paste is bioequivalent to EQUIOXX Injection. Thus, additional field studies were not performed to support the effectiveness of EQUIOXX Injection.

In controlled field studies, 127 horses (ages 3 to 37 years) were evaluated for efficacy when given EQUIOXX (firocoxib) Oral Paste for Horses at a dose of 0.045 mg/kg (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.

The material safety data sheet (MSDS) contains more detailed occupational safety information. To obtain a material safety data sheet, please call 1-877-F27-3543.

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 vomiting. Various adverse reactions associated with this drug class can occur without warning, and so 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: 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 T_{max} = 2.02 hours). The average plasma concentration following intravenous and oral administration were similar for 2 hours post-dose, after which the concentrations proceeded to decline in parallel. The terminal elimination half-life (16-160 hours) values were not significantly different (p>0.05), with values ranging from 14.6 to 68.0 hrs (mean = 31.5 hours) for the oral paste and from 12.6 to 66.3 mean = 33.1 hours) for the intravenous solution.

The major mechanism of firocoxib in the horse is cyclooxygenase inhibition followed by glucuronidation of that metabolite. Based upon radiolabel studies, the majority of firocoxib is eliminated in the urine as the glucuronide conjugate of the cyclooxygenase metabolite. Despite a high rate of plasma protein binding (98%), firocoxib exhibits a large volume of distribution (mean Vd = 1892 mL/kg). The 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 after oral administration. Little drug amount distributes into blood cells.

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 (COX) class, non-narcotic, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic, and antipyretic activity in animal models. Based on in vitro horse data, firocoxib is a selective inhibitor of prostaglandin biosynthesis through inhibition of the inducible cyclooxygenase-2 (COX-2). 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: The effectiveness of EQUIOXX Injection was established in a biocomparability study evaluating EQUIOXX Oral Paste and EQUIOXX Injection. Thus, additional field studies were not performed to support the effectiveness of EQUIOXX Injection. 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 multicenter 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, 84.8% 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.

Animal Safety: 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) 0.02 mg/kg (LX), 0.05 kg/kg (CX), 0.27 mg/kg (CX), or 0.45 mg/kg (CX 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) 0.01 mg/kg (CX), 0.03 mg/kg (CX), or 0.05 mg/kg (CX the recommended dose). This sequence five days of EQUIOXX Injection followed by nine days of EQUIOXX Oral Paste, for a total of 14 days was repeated three times for a total treatment duration of 42 days (CX the recommended treatment duration of 14 days).

Two male 54 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 (GPT or AST) were noted in all study groups at one or more timepoints. One male 3X horse with an elevated GPT value on Day 43 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.

Storage: Store at 20-25 °C with excursions between 15-35 °C.

How Supplied: EQUIOXX (firocoxib) Injection for Horses will be supplied in sterile, 25 mL amber glass vials for multi-dose use.


3 Data on file.

Manufactured for: Merial Limited Duluth, GA 30098-4640, U.S.A. 1-877-237-5043

Made in Germany

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