Non-steroidal anti-inflammatory drug for intravenous use in horses only.

**Description:** EQUIOXX (firocoxib) belongs to the cyclooxygenase-2 (COX-2) class of non-steroidal anti-inflammatory drugs (NSAIDs). Firocoxib is a white crystalline compound described chemically as 2-cyclopropylmethyl-5-(4-fluorophenyl)-4H-1,2,4-triazole-3,5-dione. The empirical formula is C₂₄H₂₃FNO₅S, and the molecular weight is 336.42. The structural formula is shown below:

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 glycerol formal.

**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 prescription. 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 can be used at a dosage of 0.045 mg/kg (0.1 mg/kg) body weight for up to an additional 9 days of treatment. The overall duration of treatment with EQUIOXX Injection and EQUIOXX Oral Paste will be dependent 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 a non-aqueous solution and should not be mixed with aqueous solutions (Do not flush through intravenous lines using aqueous flush solutions).

**Contraindications:** Horses with hypersensitivity to firocoxib should not receive EQUIOXX Injection. Warnings: For intravenous use in horses only. Do not use in horses intended for human consumption.

**Horse Warnings:** Not for use in horses. Keep this and all medications out of the reach of children. Consult a veterinarian 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:** Clients should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests should be conducted to establish hemostatic 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 to give 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 in sign such as anaphylaxis, colic, abnormal foals, or lethargy are observed. As a class, cyclo-oxygenase 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 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 effect of anticoagulant drugs. Horses should be well hydrated, and a fluid challenge is recommended before initiating treatment with NSAIDs.

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 has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

The safety of 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 corticosteroids.

**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 safety 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 adverse reactions and the clinical signs associated with NSAID intolerance. Adverse reactions may include emesis and ulcers of the gum, tongue, lips and face, weight loss, colic, diarrhea, or colitis. Various 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.

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

**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 1 = 2.02 hours). The average plasma concentrations following firocoxib injection and oral administration were similar for 2 hours post-dose, after which the concentrations proceeded to decline in parallel. The terminal elimination half-life (T1/2) 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 68.0 (mean = 33.0 hours) for the intravenous solution.

The major mechanism of firocoxib in the horse is cyclo-oxygenase inhibition followed by glucuronidation of that metabolite. Firocoxib is a selective inhibitor of prostaglandin biosynthesis through inhibition of the inducible cyclooxygenase-2 isozyme (COX-2). Firocoxib selectivity for the constitutive isozyme, 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. 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 administrated 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.

**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) 0.09 mg/kg (1X), 0.27 mg/kg (3X), or 0.45 mg/kg (5X the recommended dose). This was followed by oral 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 Oral 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).

By 42 days, 85% of horses demonstrated a white focus in the renal cortex which correlated with tubulointerstitial nephropathy microscopically. The prevalence of tubulointerstitial nephropathy was considered treatment-related.

One animal 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 (ALT or AST) were noted in all study groups at one or more timepoints. One male 3X horse with an elevated ALT 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 15-30°C.


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