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-(cyclopropylmethylene)-4-(4-(methylsulfonyl)phenyl)-5,5-dimethylfuranone. The empirical formula is C_{27}H_{27}NO_6, and the molecular weight is 438.4. 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 osteoarthropathy 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) once daily for 14 days. In target animal safety studies, toxicity was seen at the recommended dose when the duration of treatment exceeded 30 days. 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-lb increment (the body weight is an exact 50-lb 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 illustration.

2) Lock the ring in place by making ¼ turn to the right. Ensure it is locked (it should not move any further).

**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.

**Percutaneous:** Horses should undergo a thorough history and physical examination before initiation of NSAID therapy.

For technical assistance or to report suspected adverse events, call 1-877-217-3543.

**Concurrent administration of potentially nephrotoxic drugs should be carefully approached or avoided. NSAIDs may inhibit the metabolism of other NSAIDs.**

**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.

**Clinical Pharmacokinetics:**

EQUIOXX Oral Paste was safely used concomitantly with a number of other NSAIDs, and no adverse reactions were observed. Horses may have experienced more than one of the observed adverse reactions during the study.

**Information for Owner or Person Treating Horse:** You should have 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 oedema and ulcers of the gums, tongue, lips and face, weight loss, colic, diarrhoea, and 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.

**Adverse Reactions Seen in U.S. Field Studies**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>EQUIOXX (n=137)</th>
<th>Active Control (n=139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Exercise</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Lameness</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Loose stool</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Polyuria</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>

EQUIOXX (firocoxib) Oral Paste was safely used concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics, during the field studies. The material safety data sheet (MSDS) contains more detailed occupational safety information. To obtain a material safety data sheet, please call 1-877-217-3543.

**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 inappetence, colic, abnormal facies, or lethargy are observed.

As a class, cyclooxygenase inhibitors NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-related adverse events varies with the individual patient. Horses that have experienced adverse reactions from other NSAIDs may experience adverse reactions from any 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-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 perforations, concurrent use of EQUIOXX Oral Paste with other anti-inflammatory drugs, such as 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 concomitant drugs that may inhibit the metabolism of EQUIOXX Oral Paste should be carefully approached or avoided.**

**Adverse Reactions:**

**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 study, firocoxib was administered orally to healthy adult horses (four males and castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg/kg firocoxib 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 ulcers, 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 bacular mucosal bleeding time (BMBT), and a delayed platelet 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 5X 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 castrates and one male per group at 0.125 mg/kg, 0.75 mg/kg and 1.25 mg/kg (0.5, 1.75 and 2.5X the recommended dose of 0.3 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 muzzle 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 the 12.5X groups. In addition, several 12.5X horses had elevated liver enzymes (SGD, SGT, 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 347-144 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 0.53 grams of EQUIOXX paste, sufficient to treat a 1,250-lb horse.

**Clinical Pharmacokinetics:**

EQUIOXX Oral Paste was safely used concomitantly with a number of other NSAIDs, and no adverse reactions were observed. Horses may have experienced more than one of the observed adverse reactions during the study.

**Information for Owner or Person Treating Horse:** You should have 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 oedema and ulcers of the gums, tongue, lips and face, weight loss, colic, diarrhoea, and 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.