CHEWABLE TABLETS

For oral use in dogs only.

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: PREVICOX (firocoxib) belongs to the coxib class of non-narcotic, non-steroidal anti-inflammatory drugs. 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_{5}S, and the molecular weight is 336.4. The structural formula is shown below.

Pharmacokinetics: The absolute bioavailability of PREVICOX (firocoxib) is approximately 38% when administered as a 5 mg/kg oral dose to fasted adult dogs. Firocoxib is rapidly cleared from the blood via hepatic metabolism and fecal excretion (CLSystemic = -0.4 L/hr/kg). Despite a high level of plasma protein binding (96%), firocoxib exhibits a large volume of distribution (Vd of total drug = -4.6 L/kg) and a terminal elimination half life of 7.8 hours (t1/2CV = 30%). The oral drug absorption process is highly variable among subjects. Co-administration of PREVICOX with food delays drug absorption (Tmax from 1 to 5 hours) and decreases peak concentrations (Cmax from 1.3 to 0.9 mcg/mL). However, food does not affect the overall oral bioavailability at the recommended dose.

Indications: PREVICOX Chewable Tablets are indicated for the control of pain and inflammation associated with osteoarthritis and for the control of postoperative pain and inflammation associated with soft-tissue and orthopedic surgery in dogs.

Dosage and Administration: Always provide the Client Information Sheet with prescription. Carefully consider the potential benefits and risks of PREVICOX and other treatment options before deciding to use PREVICOX. Use the lowest effective dose for the shortest duration consistent with individual response. The recommended dosage of PREVICOX (firocoxib) for oral administration in dogs is 2.27 mg/lb (5.0 mg/kg) body weight once daily as needed for osteoarthritis and for 3 days as needed for postoperative pain and inflammation associated with soft-tissue and orthopedic surgery. The dogs can be treated with PREVICOX approximately two hours prior to surgery. The tablets are scored and dosage should be calculated in half tablet increments. PREVICOX Chewable Tablets can be administered with or without food.

Contraindications: Dogs with known hypersensitivity to firocoxib should not receive PREVICOX.

Warnings: Not for use in humans. Keep this and all medications out of the reach of children. Consult a veterinarian in case of accidental ingestion by humans.

For oral use in dogs only. Use of this product at doses above the recommended 2.27 mg/lb (5.0 mg/kg) in puppies less than seven months of age has been associated with serious adverse reactions, including death (see Animal Safety). Due to tablet sizes and scoring, dogs weighing less than 12.5 lb (5.7 kg) cannot be accurately dosed.

All dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum baseline data is recommended prior to and periodically during administration of any NSAID. Owners should be advised to observe for signs of potential drug toxicity (see Adverse Reactions and Animal Safety) and be given a Client Information Sheet about PREVICOX Chewable Tablets.

For technical assistance or to report suspected adverse events, call 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

Precautions: This product cannot be accurately dosed in dogs less than 12.5 pounds in body weight.

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

As a class, cyclooxygenase inhibitory NSAIDs may be associated with renal, gastrointestinal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs 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 concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached and monitored. 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 appropriately addressed. Since NSAIDs possess the potential to produce gastrointestinal ulceration and/or gastrointestinal perforation, concomitant use of PREVICOX Chewable Tablets with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. The concomitant use of protein-bound drugs with PREVICOX Chewable Tablets has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant, and behavioral medications. The influence of concomitant drugs that may inhibit the metabolism of PREVICOX Chewable Tablets has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

If additional pain medication is needed after the daily dose of PREVICOX, a non-NSAID class of analgesic may be necessary.

Appropriate monitoring procedures should be employed during all surgical procedures. Anesthetic drugs may affect renal perfusion, approach concomitant use of anesthetics and NSAIDs cautiously. The use of parenteral fluids during surgery should be considered to decrease potential renal complications when using NSAIDs peripheratively.

The safe use of PREVICOX Chewable Tablets in pregnant, lactating or breeding dogs has not been evaluated. Dogs may have experienced more than one of the observed adverse reactions during the study.

Adverse Reactions:

Osteoarthritis: In controlled field studies, 128 dogs (ages 11 months to 15 years) were evaluated for safety when given PREVICOX Chewable Tablets at a dose of 2.27 mg/lb (5.0 mg/kg) orally once daily for 30 days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed adverse reactions during the study.

Adverse Reactions Seen in the U.S. Field Studies

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>PREVICOX (n=128)</th>
<th>Active Control (n=121)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Decreased Appetite or Anorexia</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Lethargy</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Pain</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Salivation</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

PREVICOX (firocoxib) Chewable Tablets were safely used during field studies concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics.

Soft-tissue Surgery: In controlled field studies evaluating soft-tissue postoperative pain and inflammation, 256 dogs (ages 10.5 weeks to 16 years) were evaluated for safety when given PREVICOX Chewable Tablets at a dose of 2.27 mg/lb (5.0 mg/kg) orally approximately 2 hours prior to surgery and once daily thereafter for up to two days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed reactions during the study.

Adverse Reactions Seen in the Soft-tissue Surgery Postoperative Pain Field Studies

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Firocoxib Group (n=127)</th>
<th>Control Group* (n=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Bruising at Surgery Site</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory Arrest</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Sore Crespitus in Ear and Hank</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Swollen Paw</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Sham-dosed (pilled).

Orthopedic Surgery: In a controlled field study evaluating orthopedic postoperative pain and inflammation, 226 dogs of various breeds, ranging in age from 1 to 11.9 years in the PREVICOX-treated groups and 0.7 to 17 years in the control group were evaluated for safety. Of the 226 dogs, 118 were given PREVICOX Chewable Tablets at a dose of 2.27 mg/lb (5.0 mg/kg) orally approximately 2 hours prior to surgery and once daily thereafter for a total of three days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed reactions during the study.

Adverse Reactions Seen in the Orthopedic Surgery Postoperative Pain Field Study

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Firocoxib Group (n=118)</th>
<th>Control Group* (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2**</td>
<td>1</td>
</tr>
<tr>
<td>Bruising at Surgery Site</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hypersensitivity/ Decreased Appetite</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Incision Swelling, Redness</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Oozing Incision</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*Sham-dosed (pilled).
**One dog had hemorrhagic gastroenteritis.

Post Approval Experience (Rev. 2009): The following adverse reactions are based on post-approval adverse drug event reporting. The categories are listed in decreasing order of frequency by body system:

Gastrointestinal: Vomiting, anorexia, diarrhea, melena, gastrointestinal perforation, hematemesis, hematemachia, weight loss, gastrointestinal ulceration, peritonitis, abdominal pain, hypersalivation, nausea
Urinary: Elevated BUN, elevated creatinine, polyuria, polydypsia, hematuria, urinary incontinence, proteinuria, kidney failure, azotemia, urinary tract infection
Neurological / Behavioral / Special Sense: Depression/lethargy, ataxia, seizures, nervousness, confusion, weakness, hyperactivity, tremor, paresis, head tilt, nystagmus, mydriasis, aggression, uveitis

Owners should be given a Client Information Sheet about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

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Hepatic: Elevated ALP, elevated ALT, elevated bilirubin, decreased albumin, elevated AST, icterus, decreased or increased total protein and globulin, pancreatitis, ascites, liver failure, decreased BUN

Hematological: Anemia, neutrophilia, thrombocytopenia, neutropenia

Cardiovascular / Respiratory: Tachypnea, dyspnea, tachycardia

Dermatologic/Immunologic: Pruritus, fever, alopecia, moist dermatitis, autoimmune hemolytic anemia, facial/muzzle edema, urticaria

In some cases, death has been reported as an outcome of the adverse events listed above.

For technical assistance or to report suspected adverse events, call 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

Information For Dog Owners: PREVICOX, like other drugs of its class, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, restlessness, or behavioral changes. Owners should be advised of the importance of periodic follow-up for all dogs during administration of any NSAID.

Clinical Pharmacology: Mode of action: PREVICOX (firocoxib) is a cyclooxygenase-inhibiting (coxib) class, non-steroidal, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory and analgesic properties. There are two main cyclooxygenase enzymes, COX-1 and COX-2, and a newly discovered class, non-narcotic, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory and analgesic properties. There are two main cyclooxygenase enzymes, COX-1 and COX-2, and a newly discovered class, non-narcotic, non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory and analgesic properties.

In the 3X dose group, one dog had谩a decreased serum albumin. At study completion, of five surviving and clinically normal 3X dogs, three had minimal peripheral hepatic fatty change. Of twelve dogs in the 5X dose group, one dog died (Day 92) and three moribund dogs were euthanized (Days 38, 78, and 79) because of anorexia, poor weight gain, depression, and in one dog, vomiting. One of the euthanized dogs had ingested a rope toy. Two of these 5X dogs had mildly elevated liver enzymes. At necropsy all five of the dogs that died or were euthanized had moderate peripheral or severe panzonal hepatic fatty change; two had moderate edema; and two had panzonal edema. Of two other clinically normal 5X dogs (out of four euthanized as comparators to the clinically affected dogs), one had slight and one had moderate peripheral hepatic fatty change. Drug treatment was discontinued for four dogs in the 5X group. These dogs survived the remaining 14 weeks of the study. On average, the dogs in the 3X and 5X dose groups did not gain as much weight as control dogs. Rate of weight gain was measured (instead of weight loss) because these were young growing dogs. Thalamic vacuolation was seen in three of six dogs in the 3X dose group, five of twelve dogs in the 5X dose group, and to a lesser degree in two unmedicated controls.

In a separate dose tolerance safety study involving a total of six dogs (two control dogs and four treated dogs), firocoxib was administered to four healthy adult Beagle dogs at 50 mg/kg (ten times the recommended daily dose) for twenty-two days. All dogs survived to the end of the study. Three of the four treated dogs developed small intestinal erosion or ulceration. Treated dogs that developed small intestinal erosion or ulceration had a higher incidence of vomiting, diarrhea, and decreased food consumption than control dogs. One of these dogs had severe duodenal ulceration, with hepatic fatty change and associated vomiting, diarrhea, anorexia, weight loss, ketonuria, and mild elevations in AST and ALT. All four treated dogs exhibited progressively decreasing serum albumin that with the exception of one dog that developed hypobulinemia, remained within normal range. Mild weight loss also occurred in the treated group. One of the two control dogs and three of the four treated dogs exhibited transient increases in ALP that remained within normal range.

Storage: Store at room temperature, between 59°–86° F (15°–30° C). Brief periods up to 104° F (40° C) are permitted.

To Request a Safety Data Sheet (SDS), call 1-888-637-4251.

How Supplied: PREVICOX is available as round, beige to tan, half-scored tablets in two strengths, containing 57 mg or 227 mg firocoxib. Each tablet strength is supplied in 3-count, 10-count and 30-count blister packages and 60-count and 180-count bottles.


4 Zhang, et al., Inhibition of Cyclo-oxygenase-2 Rapidly Reduces Inflammation Hypertension and Preeclampsia. JUPTZ 1997;265:1069-1075.

5 Jones and Budsberg, pp. 721-729.

6 Zhang, et al., pp. 1069-1075.


8 Data on file.

Made in France

Marketed by: Boehringer Ingelheim Animal Health USA Inc., Duluth, GA 30096. 1-888-637-4251

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