Veterinary Physician's Prescribing Information

PREVICOX 57 MG and 227 MG VETERINARY

1. TRADE NAME OF MEDICINAL PRODUCT
PREVICOX 57 MG VETERINARY
PREVICOX 227 MG VETERINARY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each chewable tablet contains:

Trade name of medicinal product:	Active substance:
PREVICOX 57 MG VETERINARY	Firocoxib 57 mg per chewable tablet
PREVICOX 227 MG VETERINARY	Firocoxib 227 mg per chewable tablet

Excipients: Iron Oxides (E172) and Caramel (E150d).
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Chewable tablets.
Tan-brown, round, convex, tablets with a cross-shaped break line on one side. The tablets can be divided into 2 or 4 equal parts.

4. CLINICAL PARTICULARS
4.1 Target species: Dogs.

4.2 Indications for use, specifying the target species:
For the relief of pain and inflammation associated with osteoarthritis in dogs.
For the relief of post-operative pain and inflammation associated with soft-tissue surgery in dogs.
For the relief of post-operative pain and inflammation associated with orthopaedic and dental surgery in dogs.

4.3 Contraindications:
Do not use in pregnant or lactating bitches.
Do not use in animals less than 10 weeks of age or less than 3 kg body weight.
Do not use in animals suffering from gastrointestinal bleeding, blood dyscrasia or haemorrhagic disorders.
Do not use concomitantly with corticosteroids or other non-steroidal anti-inflammatory drugs (NSAIDs).

4.4 Special warnings: None.

4.5 Special precautions for use:
Special precautions for use in animals: The recommended dose, see section 4.9, should not be exceeded.
Use in very young animals, or animals with suspected or confirmed impairment of renal, cardiac or hepatic function may involve additional risk. If such use cannot be avoided, those dogs require careful veterinary monitoring.

Avoid use in dehydrated, hypovolaemic or hypotensive animals, as there is a potential risk of increased renal toxicity. Concurrent administration of potentially nephrotoxic drugs should be avoided.
Use this product under strict veterinary monitoring where there is a risk of gastrointestinal bleeding, or if the animal previously displayed intolerance to NSAIDs. Renal and/or hepatic disorders have been reported in very rare cases in dogs administered the recommended treatment dose. It is possible that a proportion of such cases had sub-clinical renal or hepatic disease prior to the commencement of therapy. Therefore, appropriate laboratory testing to establish baseline renal or hepatic biochemistry parameters is recommended prior to and periodically during administration.

The treatment should be discontinued if any of these signs are observed: repeated diarrhoea, vomiting, faecal occult blood, sudden weight loss, anorexia, lethargy, degradation of renal or hepatic biochemistry parameters.

Special precautions to be taken by the person administering the veterinary medicinal product to animals: Wash hands after use of the product.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Divided tablets should be returned to the original package.

4.6 Adverse reactions (frequency and seriousness):
Emesis and diarrhoea have occasionally been reported. These reactions are generally of a transitory nature and are reversible when the treatment is stopped. Renal and/or hepatic disorders have been reported in very rare cases in dogs administered the recommended treatment dose. Rarely, nervous system disorders have been reported in treated dogs.

If adverse reactions like vomiting, repeated diarrhoea, faecal occult blood, sudden weight loss, anorexia, lethargy, degradation of renal or hepatic biochemistry parameters occur, use of the product should be stopped and the advice of a veterinarian should be sought. As with other NSAIDs, serious adverse effects can occur and, in very rare cases, may be fatal.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated- displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit / risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:
https://sideeffects.health.gov.il /

4.7 Use during pregnancy, lactation or lay: Do not use in pregnant or lactating bitches. Laboratory studies in rabbits have shown evidence of maternotoxic and foetotoxic effects at dose rates approximating the recommended treatment dose for the dog.

4.8 Interaction with other medicinal products and other forms of interaction:
Pre-treatment with other anti-inflammatory substances may result in additional or increased adverse effects and accordingly a treatment-free period with such drugs should be observed for at least 24 hours before the commencement of treatment with PREVICOX VETERINARY. The treatment-free period, however, should take into account the pharmacokinetic properties of the products used previously.

PREVICOX VETERINARY must not be administered in conjunction with other NSAIDs or glucocorticosteroids. Gastrointestinal tract ulceration may be exacerbated by corticosteroids in animals given non-steroidal anti-inflammatory drugs.

Concomitant treatment with molecules displaying action on renal flow, e.g. diuretics or Angiotensin Converting Enzyme (ACE) inhibitors, should be subject to clinical monitoring. Concurrent administration of potentially nephrotoxic drugs should be avoided as there might be an increased risk of renal toxicity. As anaesthetic drugs may affect renal perfusion, the use of parenteral fluid therapy during surgery should be considered to decrease potential renal complications when using NSAIDs peri-operatively.

Concurrent use of other active substances that have a high degree of protein binding may compete with firocoxib for binding and thus lead to toxic effects.

4.9 Amounts to be administered and administration route:
Oral use.

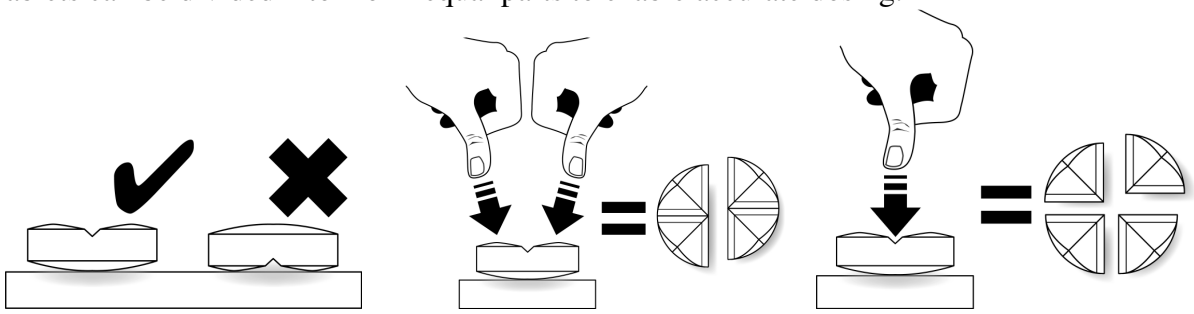
Osteoarthritis:
Administer 5 mg per kg bodyweight once daily as presented in the table below.
Tablets can be administered with or without food.
Duration of treatment will be dependent on the response observed. As field studies were limited to 90 days, longer-term treatment should be considered carefully and regular monitoring undertaken by the veterinarian.

Relief of post-operative pain:
Administer 5 mg per kg bodyweight once daily as presented in the table below for up to 3 days as needed, starting approximately 2 hours prior to surgery.
Following orthopaedic surgery and depending on the response observed, treatment using the same daily dosing schedule may be continued after the first 3 days, upon judgement of the attending veterinarian.

Body weight (kg)	**Number of chewable tablets by size**		**mg/kg range**
	57 mg	**227 mg**	
3.0 - 5.5	0.5	- - - -	5.2 - 9.5
5.6 - 7.5	0.75	- - - -	5.7 - 7.6
7.6 - 10	1	0.25	5.7 - 7.5
10.1 - 13	1.25	- - - -	5.5 - 7.1
13.1 - 16	1.5	- - - -	5.3 - 6.5
16.1 - 18.5	1.75	- - - -	5.4 - 6.2
18.6 - 22.5	- - - -	0.5	5.0 - 6.1
22.6 - 34	- - - -	0.75	5.0 - 7.5
34.1 - 45	- - - -	1	5.0 - 6.7
45.1 - 56	- - - -	1.25	5.1 - 6.3
56.1 - 68	- - - -	1.5	5.0 - 6.1
68.1 - 79	- - - -	1.75	5.0 - 5.8

79.1 - 90	- - - -	2	5.0 - 5.7

Tablets can be divided into 2 or 4 equal parts to enable accurate dosing.



Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.

To split into 2 equal parts: Press your thumbs down on both sides of the tablet.

To split into 4 equal parts: Press your thumb down in the middle of the tablet.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary: In dogs ten weeks of age, at the start of treatment, at dose rates equal or greater to 25 mg/kg/day (5 times the recommended dose) for three months, the following signs of toxicity were observed: bodyweight loss, poor appetite, changes in the liver (accumulation of lipid), brain (vacuolisation), duodenum (ulcers) and death. At dose rates equal or greater to 15 mg/kg/day (3 times the recommended dose) for six months, similar clinical signs were observed, albeit that the severity and frequency were less and duodenal ulcers were absent.
In those target animal safety studies, clinical signs of toxicity were reversible in some dogs following cessation of therapy.

In dogs seven months of age, at the start of treatment, at dose rates greater than or equal to 25 mg/kg/day (5 times the recommended dose) for six months, gastrointestinal adverse effects, i.e. vomiting were observed.

Overdose studies were not conducted in animals over 14 months of age.

If clinical signs of overdosing are observed, discontinue treatment.

4.11 Withdrawal period(s): Not applicable.

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids.
ATCvet code: QM01AH90.

5.1 Pharmacodynamic properties: Firocoxib is a non-steroidal anti-inflammatory drug (NSAID) belonging to the Coxib group, which acts by selective inhibition of cyclooxygenase-2 (COX-2) – mediated prostaglandin synthesis. Cyclooxygenase is responsible for generation of prostaglandins. COX-2 is the isoform of the enzyme that has been shown to be induced by pro-inflammatory stimuli and has been postulated to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation, and fever. Coxibs therefore display analgesic, anti-inflammatory and antipyretic properties. COX-2 is also thought to be involved in ovulation, implantation and closure of the *ductus arteriosus*, and central nervous system

functions (fever induction, pain perception and cognitive function). In *in-vitro* canine whole blood assays, firocoxib exhibits approximately 380-fold selectivity for COX-2 over COX-1. The concentration of firocoxib required to inhibit 50 % of the COX-2 enzyme (i.e., the IC50) is 0.16 (± 0.05) µM, whereas the IC50 for COX-1 is 56 (± 7) µM.

5.2 Pharmacokinetic particulars: Following oral administration in dogs at the recommended dose of 5 mg per kg of bodyweight, firocoxib is rapidly absorbed and the time to maximal concentration (Tmax) is 1.25 (± 0.85) hours. The peak concentration (Cmax) is 0.52 (± 0.22) µg/ml (equivalent to approximately 1.5 µM), area under the curve (AUC 0-24) is 4.63 (±1.91) µg x hr/ml, and oral bioavailability is 36.9 (± 20.4) percent. The elimination half-life (t½) is 7.59 (± 1.53) hours. Firocoxib is approximately 96 % bound to plasma proteins. Following multiple oral administrations, the steady state is reached by the third daily dose.
Firocoxib is metabolised predominantly by dealkylation and glucuronidation in the liver. Elimination is principally in the bile and gastrointestinal tract.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients: Lactose Monohydrate, Microcrystalline Cellulose, Chartor Hickory Smoke Flavour, Hydroxypropyl Cellulose, Croscarmellose Sodium, Magnesium Stearate, Caramel (E150d), Colloidal Silicone Dioxide, Yellow Iron Oxide (E172), Red Iron Oxide (E172).

6.2 Major incompatibilities: Not applicable.

6.3 Shelf life: The expiry date of the product is indicated on the label and packaging. Do not use after the expiry date.
Divided tablets may be stored for up to 1 month in the original package.
Shelf life after first opening the bottle pack: use the remaining tablets within 3 months.

6.4 Special precautions for storage: Store below 30°C. Store in the original package.

6.5 Nature and composition of immediate packaging: PREVICOX VETERINARY are supplied in blisters (transparent PVC /aluminium foil) or in high density polyethylene bottles (with polypropylene closure).
The chewable tablets (57 mg or 227 mg) are available in the following pack sizes:
- Cardboard box with blister strips of 10 tablets per blister. The number of blister strips per cardboard box may vary between 1 to 5 (i.e., total of 10 tablets to 50 tablets).
- Cardboard box containing 1 bottle of 60 tablets.

Not all packs sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products: Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. Israeli Drug Registration Number:
PREVICOX 57 MG VETERINARY: 144-68-92443-00
PREVICOX 227 MG VETERINARY: 144-69-92444-00

8. Manufacturer: Boehringer Ingelheim Vetmedica GmbH, Ingelheim am Rhein, Germany (by Boehringer Ingelheim Animal Health France, Toulouse, France).

9. Israeli Marketing Authorization Holder: Beit Erez Havat Milatin, VAT no. 511088106, P.O.B. 209, Mishmar Hashiva 5029700, Israel.

10) REVISED ON: 11/2021 according to MOH's guidelines.
[Internal code: PRVCX-VET-DCTR-11/21 dated 17/11/2021]