1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Rogiola 6 mg chewable tablets for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substance:
Robenacoxib 6 mg

Excipients:

Qualitative composition of excipients and other constituents
Cellulose, microcrystalline
Povidone
Crospovidone
Yeast powder
Meat flavour
Silica, colloidal anhydrous
Magnesium stearate

Light brown, round, biconvex tablets with lighter and darker dots.

3. CLINICAL INFORMATION

3.1 Target species

Cats.

3.2 Indications for use for each target species

For the treatment of pain and inflammation associated with acute or chronic musculoskeletal disorders.
For the reduction of moderate pain and inflammation associated with orthopaedic surgery.

3.3 Contraindications

Do not use in cats suffering from gastrointestinal ulceration.
Do not use concomitantly with corticosteroids or other non-steroidal anti-inflammatory drugs (NSAIDs).
Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in pregnant and lactating animals (see section 3.7).

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

The safety of the veterinary medicinal product has not been established in cats weighing less than 2.5 kg or under 4 months of age.

Use in cats with impaired cardiac, renal or hepatic function or in cats that are dehydrated, hypovolaemic or hypotensive may involve additional risks. If use cannot be avoided, these cats require careful monitoring.

Response to treatment should be monitored at regular intervals by a veterinary surgeon. Clinical field studies showed that robenacoxib was well-tolerated by most cats for up to 12 weeks.

Use this veterinary medicinal product under strict veterinary monitoring in cats with a risk of gastrointestinal ulcers, or if the cat previously displayed intolerance to other NSAIDs.

Tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

For pregnant women, particularly near-term pregnant women, prolonged dermal exposure increases the risk of premature closure of the ductus arteriosus in the foetus. Pregnant women should take special care to avoid accidental exposure.

Accidental ingestion increases the risk for NSAID adverse effects, particularly in small children. Care should be taken to avoid accidental ingestion by children. In order to prevent children from accessing the product, do not remove tablets from the blister until ready to administer to the animal.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use of the veterinary medicinal product.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cats:

Common (1 to 10 animals / 100 animals treated):	Diarrhoea[1], Vomiting[1]
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Elevated renal parameters (creatinine, BUN, and SDMA)[2] Renal insufficiency[2] Lethargy

[1]Mild and transient.
[2]More commonly in older cats and with concomitant use of anaesthetic or sedative agents.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

The safety of the veterinary medicinal product has not been established in cats used for breeding.

Pregnancy and lactation:
Do not use during pregnancy and lactation.

Fertility:
Do not use in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

This veterinary medicinal product must not be administered in conjunction with other NSAIDs or glucocorticosteroids. Pre-treatment with other anti-inflammatory medicines may result in additional or increased adverse effects and, accordingly, a treatment-free period with such substances should be observed for at least 24 hours before the commencement of treatment with this veterinary medicinal product. The treatment-free period, however, should take into account the pharmacokinetic properties of the products used previously.

Concomitant treatment with medicines displaying action on renal flow, e.g. diuretics or angiotensin-converting enzyme (ACE) inhibitors, should be subject to clinical monitoring. In healthy cats treated with or without the diuretic furosemide, concomitant administration of this veterinary medicinal product with the ACE inhibitor benazepril for 7 days was not associated with any negative effects on plasma aldosterone concentrations, plasma renin activity or glomerular filtration rate. No safety data in the target population and no efficacy data in general exist for the combined treatment of robenacoxib and benazepril.

As anaesthetics 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 administration of potentially nephrotoxic medicines should be avoided as there might be an increased risk of renal toxicity.

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

3.9 Administration routes and dosage

Oral use.

Give either without food or with a small amount of food. The tablets should not be divided or broken.

The recommended dose of robenacoxib is 1 mg/kg body weight with a range 1-2.4 mg/kg. The following number of tablets should be given once daily at the same time every day:

Body weight (kg)	Number of tablets
2.5 to < 6	1 tablet
6 to 12	2 tablets

Acute musculoskeletal disorders: treat for up to 6 days.

Chronic musculoskeletal disorders: Duration of treatment should be decided by the responsible veterinarian on an individual basis. Please refer to section 3.5.

A clinical response is normally seen within 3-6 weeks. Treatment should be discontinued after 6 weeks if no clinical improvement is apparent.

Orthopaedic surgery: Give as a single oral treatment prior to orthopaedic surgery.
Premedication should only be carried out in combination with butorphanol-analgesia. The tablet(s) should be administered without food at least 30 minutes prior to surgery.

After surgery, once daily treatment may be continued for up to two further days. If necessary, additional analgesic treatment with opioids is recommended.
The interchangeable use of the veterinary medicinal product in the form of tablets and solution for injection has been tested in a target animal safety study and was shown to be well tolerated by cats.

For cats, the veterinary medicinal products containing robenacoxib in the form of solution for injection or tablets may be used interchangeably in accordance with the indications and directions of use approved for each pharmaceutical form. Treatment should not exceed one dose (either tablet or injection) per day. Please note that the recommended doses for the two formulations may be different.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

In healthy young cats aged 7-8 months, oral robenacoxib administered at high overdoses (4, 12 or 20 mg/kg/day for 6 weeks) did not produce any signs of toxicity, including no evidence of any gastrointestinal, kidney or liver toxicity and no effect on bleeding time.

In healthy young cats aged 7-8 months, oral robenacoxib (tablets) administered at overdoses of up to 5 times the maximum recommended dose (2.4 mg, 7.2 mg, 12 mg robenacoxib/kg bodyweight) for 6 months was well tolerated. A reduction in body weight gain was observed in treated animals. In the high dose group kidney weights were decreased and sporadically associated with renal tubular degeneration/regeneration but not correlated with evidence of renal dysfunction on clinical pathology parameters.

The interchangeable use of veterinary medicinal products containing robenacoxib in the form of tablets and solution for injection in 4-month-old cats at overdoses of up to 3 times the maximum recommended dose (2.4, 4.8 and 7.2 mg robenacoxib/kg orally and 2.0 mg, 4.0 mg and 6.0 mg robenacoxib/kg subcutaneously) resulted in a dose-dependent increase of sporadic oedema at the injection site and minimal to mild subacute/chronic inflammation of the subcutaneous tissue. A dose-dependent increase in the QT interval, a decreased heart rate and corresponding increased respiratory rate were observed in laboratory studies. No relevant effects on body weight, bleeding time or evidence of any gastrointestinal, kidney or liver toxicity were observed.

In overdose studies conducted in cats, there was a dose-dependent increase in the QT interval. The biological relevance of increased QT intervals outside of normal variations observed following overdose of robenacoxib is unknown. No changes in the QT interval were observed after single intravenous administration of 2 or 4 mg/kg robenacoxib to anaesthetised healthy cats.

As with any NSAID, overdose may cause gastrointestinal, kidney, or liver toxicity in sensitive or compromised cats. There is no specific antidote. Symptomatic supportive therapy is recommended and should consist of administration of gastrointestinal protective agents and infusion of isotonic saline.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code :

QM01AH91.

4.2 Pharmacodynamics

Robenacoxib is a non-steroidal anti-inflammatory drug (NSAID) of the coxib class. It is a potent and selective inhibitor of the cyclooxygenase 2 enzyme (COX-2). The cyclooxygenase enzyme (COX) is present in two forms. COX-1 is the constitutive form of the enzyme and has protective functions, e.g. in the gastrointestinal tract and kidneys. COX-2 is the inducible form of the enzyme which is responsible for the production of mediators including PGE2 which induce pain, inflammation or fever.

In the *in vitro* whole blood assay in cats, the selectivity of robenacoxib was approximately 500 fold higher for COX-2 (IC_{50} 0.058 µM) as compared to COX-1 (IC_{50} 28.9 µM). At a dose of 1-2 mg/kg body weight, robenacoxib tablets produced a marked inhibition of COX-2 activity in cats and had no effect on COX-1 activity. In an inflammation model in cats, robenacoxib injection had analgesic, anti-inflammatory and anti-pyretic effects and a rapid onset of action (0.5 h). In clinical trials in cats, robenacoxib tablets reduced pain and inflammation associated with acute musculoskeletal disorders and reduced the need for rescue treatment when given as premedication in case of orthopaedic surgery, in combination with opioids. In two clinical trials in (mainly indoor) cats with chronic musculoskeletal disorder (CMSD), robenacoxib increased the activity and improved subjective scores of activity, behaviour, quality of life, temperament and happiness of the cats. Differences between robenacoxib and placebo were significant ($P<0.05$) for the client specific outcome measures, but did not reach significance ($P=0.07$) for the feline musculoskeletal pain index.

In a clinical study, 10 of 35 CMSD cats were assessed to be significantly more active when treated with robenacoxib for three weeks compared to these same cats when they received a placebo treatment. Two cats were more active when given placebo and for the remaining 23 cats no significant difference in activity could be detected between robenacoxib and placebo treatment.

4.3 Pharmacokinetics

Absorption
After oral administration of robenacoxib tablets at approximately 2 mg/kg without food, peak blood concentrations are attained rapidly with a T_{max} of 0.5 h, a C_{max} of 2,713 ng/ml and an AUC of 2,488 ng·h/ml. Co-administration of robenacoxib tablets with one third of the daily food ration produced no change in T_{max}, C_{max} or AUC. Co-administration of robenacoxib tablets with the entire daily food ration produced no delay in T_{max}, but a lower C_{max} and a slightly lower AUC. The systemic bioavailability of robenacoxib tablets was 49% without food.

Distribution
Robenacoxib has a relatively small volume of distribution (Vss 190 ml/kg) and is highly bound to plasma proteins (>99%).

Biotransformation
In cats robenacoxib is extensively metabolised by the liver. Apart from one lactam metabolite, the identity of other metabolites is not known in cats.

Elimination
Robenacoxib is rapidly cleared from blood (CL 0.44 L/kg/h) with an elimination $t_{1/2}$ of 1.1 h after intravenous administration. After oral administration of tablets, the terminal half-life from blood was 1.59 h. Robenacoxib persists longer and at higher concentrations at sites of inflammation than in blood. Robenacoxib is excreted predominantly via the biliary route (~70%) rather than via the kidneys (~30%). The pharmacokinetics of robenacoxib do not differ between male and female cats.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

5.3 Special precautions for storage

Do not store above 30 °C. Store in the original package in order to protect from moisture.

5.4 Nature and composition of immediate packaging

OPA/Al/PVC/Aluminium blisters containing 6 or 10 tablets.

Pack sizes:
Cardboard box with 1 blister of 6 tablets (6 tablets).
Cardboard box with 1 blister of 10 tablets (10 tablets).
Cardboard box with 3 blisters of 10 tablets (30 tablets).
Cardboard box with 6 blisters of 10 tablets (60 tablets).

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

KRKA, d.d., Novo mesto

7. MARKETING AUTHORISATION NUMBER(S)

VPA10774/076/005

8. DATE OF FIRST AUTHORISATION

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).