1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Robentrol 6mg tablets for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Robenacoxib 6.0 mg

Excipients:

Qualitative composition of excipients and other constituents
Yeast flavour powder
Microcrystalline cellulose PH101
Microcrystalline cellulose PH102
Povidone (PVP) K 30
Crospovidone
Silica, colloidal anhydrous
Magnesium stearate

Round biconvex, beige to brown coloured tablets with embossing "C6" on one side and plain on the other side.

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 pregnant and lactating animals or in cats used for breeding.
Do not use in cases of hypersensitivity to the active substance or to any of the excipient(s).

3.4 Special warnings for each target species

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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

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.

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. Tablets should be administered and stored (in the original packaging) out of sight and reach of children.
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

Cat:

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

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

Fertility:
The safety of the veterinary medicinal product has not been established in cats used for breeding. Do not use in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

The 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 the 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 the 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. These tablets are easy to administer and well accepted by most cats. The tablets should not be divided or broken.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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 on an individual basis. 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.

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 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.

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.

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 PGE_2 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 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

In cat, after oral administration of robenacoxib tablets at approximately 2 mg/kg bw without food, peak blood concentrations are attained rapidly with a T_{max} of 0.5 h, a C_{max} of 2159 ng/mL and an AUC of 2099 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 Tmax, but a lower Cmax and a slightly lower AUC. The systemic bioavailability of robenacoxib tablets was 49% without food.

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

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

After oral administration of tablets, the terminal half-life from blood was 0.82 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

Store below 25 °C.
Store in the original package.

5.4 Nature and composition of immediate packaging

Blister packs made of cold form laminate of OPA/ALU/PVC with an aluminium foil with 6 tablet/blister in a cardboard box.

Pack sizes:
Cardboard box with 6 tablets.
Cardboard box with 12 tablets.
Cardboard box with 18 tablets.
Cardboard box with 24 tablets.
Cardboard box with 30 tablets.
Cardboard box with 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

Chanelle Pharmaceuticals Manufacturing Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA10987/184/001

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).