1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Robentrol 20 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:

Robenacoxib 20.0mg

Excipients:

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

Round biconvex, beige to brown coloured tablets, with embossing "C20" on one side and plain on the other side.

3. CLINICAL INFORMATION

3.1 Target species

Dogs (≥5kg)

3.2 Indications for use for each target species

For the treatment of pain and inflammation associated with chronic osteoarthritis.
For the treatment of pain and inflammation associated with soft tissue surgery.

3.3 Contraindications

Do not use in dogs suffering from gastrointestinal ulceration or with hepatic disease.
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 or in dogs used for breeding.

3.4 Special warnings for each target species

In clinical studies in dogs with osteoarthritis, inadequate response to treatment was seen in 10–15% of the dogs.

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 dogs weighing less than 2.5 kg or under 3 months of age.

For long term therapy, liver enzymes should be monitored at the start of therapy, e.g. after 2, 4 and 8 weeks. Thereafter it is recommended to continue regular monitoring, e.g. every 3–6 months. Therapy should be discontinued if liver enzyme activities increase markedly or the dog shows clinical signs such as anorexia, apathy or vomiting in combination with elevated liver enzymes.

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

Use this product under strict veterinary monitoring in dogs with a risk of gastrointestinal ulcers, or if the dog 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

Dog:

Very common (>1 animal / 10 animals treated):	Digestive tract disorder[1], Diarrhoea, Vomiting
Common (1 to 10 animals / 100 animals treated):	Decreased appetite Elevated liver enzymes[2]
Uncommon (1 to 10 animals / 1,000 animals treated):	Blood in faeces
Very rare (< 1 animal / 10 000 animals treated, including isolated reports):	Lethargy

[1] Most cases were mild and recovered without treatment.

[2] In dogs treated up to 2 weeks, there were no increase in liver enzyme activities observed. However, with long-term treatment, increases in liver enzyme activities were reported. In most cases there were no clinical signs and

the liver enzyme activities either stabilised or decreased with continued treatment. Increases in liver enzyme activities associated with clinical signs of anorexia, apathy or vomiting were uncommon.

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 dogs used for breeding. 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 glucocorticoids. 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 dogs treated with and 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 urine 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.

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.

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

Osteoarthritis:
The recommended dose is one tablet for a dog weighing from 10 kg to 20 kg (*i.e.* 1 mg of robenacoxib per kg body weight with a range 1–2 mg of robenacoxib per kg body weight).

Administer once daily at the same time every day according to the table below.

Body weight (kg)	Number of tablets
10 to < 20	1 tablet

Do not administer with food since clinical trials demonstrated better efficacy of robenacoxib for osteoarthritis when administered without food or at least 30 minutes before or after a meal.

A clinical response is normally seen within a week. Treatment should be discontinued after 10 days if no clinical improvement is apparent.
For long-term treatment, once a clinical response has been observed, the dose of the veterinary medicinal product can be adjusted to the lowest effective individual dose reflecting that the degree of pain and inflammation associated with chronic osteoarthritis may vary over time. Regular monitoring should be undertaken by the veterinarian**.**

Soft tissue surgery:
The recommended dose of robenacoxib is one tablet for a dog weighing from 5 to 10 kg (*i.e.* 2 mg of robenacoxib per kg body weight with a range of 2-4 mg/kg body weight).

Give as a single oral treatment prior to soft tissue surgery according to the table below.

Body weight (kg)	Number of tablets
5 to < 10	1 tablet

The tablets 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.

These tablets are flavoured and are taken voluntarily by most dogs. The tablets should not be divided or broken.

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

In healthy young dogs aged 5–6 months, oral robenacoxib administered at high overdoses (4, 6 or 10 mg/kg/day for 6 months) did not produce any signs of toxicity, including no evidence of any gastrointestinal, kidney or liver toxicity and no effect on bleeding time. Robenacoxib also had no detrimental effects on cartilages or joints.

As with any NSAID, overdose may cause gastrointestinal, kidney, or liver toxicity in sensitive or compromised dogs. There is no specific antidote. Symptomatic, supportive therapy is recommended consisting 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 and is responsible for the production of mediators including PGE_2 which induce pain, inflammation or fever.

In an *in vitro* whole blood assay in dogs, robenacoxib was approximately 140 fold selective for COX-2 (IC_{50} 0.04 μM) as compared to COX-1 (IC_{50} 7.9 μM). Robenacoxib produced marked inhibition of COX-2 activity and had no effect on COX-1 activity in dogs at oral doses ranging from 0.5 to 4 mg/kg. Robenacoxib tablets are therefore COX-1 sparing at recommended doses in dogs. Robenacoxib had analgesic and anti-inflammatory actions in an inflammation model in dogs with single oral doses ranging from 0.5 to 8 mg/kg, with an ID_{50} of 0.8 mg/kg and a rapid onset of action (0.5 h). In clinical trials in dogs, robenacoxib reduced the lameness and inflammation associated with chronic osteoarthritis, and pain, inflammation and the need for rescue treatment in dogs undergoing soft tissue surgery.

4.3 Pharmacokinetics

In dog, after oral administration of robenacoxib tablets at 4 mg/kg bw without food, peak blood concentrations are attained rapidly with a Tmax of 0.75 h, a C_{max} of 3349 ng/mL and an AUC of 4725 ng·h/mL. Co-administration of robenacoxib tablets with food produced no delay in Tmax, but slightly lower values for C_{max} and AUC. The systemic bioavailability of robenacoxib tablets in dogs was 62 % with food and 84 % without food.

Robenacoxib has a relatively small volume of distribution (Vss 240 mL/kg) and is highly bound to plasma proteins (> 99 %).

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

After oral administration of the tablets, the terminal half-life in blood was 2.11 h. Robenacoxib persists longer and at higher concentrations at sites of inflammation than in blood. Robenacoxib is excreted predominantly *via* the biliary route (~ 65 %) and the remainder *via* the kidneys. Repeated oral administration of robenacoxib to dogs at dosages of 2–10 mg/kg bw for 6 months produced no change in the blood profile, with neither accumulation of robenacoxib nor enzyme induction. Accumulation of metabolites has not been tested. The pharmacokinetics of robenacoxib do not differ between male and female dogs and are linear over the range 0.5–8 mg/kg bw.

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 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)

VPA10987/183/003

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).