[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Duecoxin 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
Maize starch pregelatinised
Yeast
Povidone K-30 (E1201)
Magnesium stearate
Silica, colloidal anhydrous (E551)
Crospovidone (E1202)
Liver flavour
Cellulose, microcrystalline (E460)

Oblong whitish tablet, with one break-mark. The tablet can be divided in two equal parts.

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 cases 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.

The 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.
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

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, blood urea nitrogen (BUN) and symmetrical dimethylarginine (SDMA))[2] Renal insuffiency [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.

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

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

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 cats 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 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

For oral use.

Give either without food or with a small amount of food. The tablets are easy to administer and well accepted by most cats. The tablets can divided in two equal parts along the designated score line.

The recommended dose of robenacoxib is 1 mg/kg body weight with a range 1–2.4 mg/kg. The dose should be given once daily at the same time every day, according to the following table:

Body weight (Kg)	Number of tablets 6 mg
2,5 to 3	½
> 3 to 6	1
> 6 to 9	1 + ½
> 9 to 12	2

Acute musculoskeletal disorders: treat for up to 6 days.

Chronic musculoskeletal disorders: duration of treatment should be decided 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.

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 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 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
DOSE OF 2 MG/KG
In a study, 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 1,159 ng/ml and an AUC of 1,337 ng·h/ml. Co-administration of robenacoxib tablets with one third of the daily food ration produced no change in T_{max} (0.5h), C_{max} (1,201 ng/ml) or AUC (1383 ng·h/ml). Co-administration of robenacoxib tablets with the entire daily food ration produced no delay in T_{max} (0.5 h), but a lower C_{max} (691 ng/ml) and a slightly lower AUC (1,069 ng·h/ml). The systemic bioavailability of robenacoxib tablets was 49% without food.

DOSE OF 1.5 MG/KG
After an oral administration of robenacoxib tablets at approximately 1,5 mg/kg with one third of the daily food ration, a T_{max} of 1.17 h, a C_{max} of 1,229.68 ng/ml and an AUC_{last} of 2,360.24 ng·h/ml. were observed.

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 the tablets, the terminal half-life in blood was 1.7 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: 3 years.
Shelf life of halved tablets: 1 day.

5.3. Special precautions for storage

Store below 25 °C.
Keep the blister in the outer carton in order to protect from moisture.
Any unused divided tablet portion should be returned into the blister, kept within the outer carton.

5.4. Nature and composition of immediate packaging

Blister in PVC/PE/PVdC/PE/PVC sealed with thermoheated lacquered aluminium foil containing 10 chewable tablets, in a cardboard box.

Package sizes:
Cardboard box with 1 blister (10 chewable tablets)
Cardboard box with 3 blisters (30 chewable tablets)
Cardboard box with 10 blisters (100 chewable 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

Fatro S.p.A.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box:
1 blister x 10 tablets
3 blisters x 10 tablets
10 blisters x 10 tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Duecoxin 6 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCE

Each chewable tablet contains Robenacoxib 6 mg.

3. PACKAGE SIZE

10 tablets
30 tablets
100 tablets

4. TARGET SPECIES

Cats

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once divided use within 1 day.

9. SPECIAL STORAGE PRECAUTIONS

Store below 25 °C.
Keep the blister in the outer carton in order to protect from moisture.
Any unused divided tablet portion should be returned into the blister, kept within the outer carton.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Fatro S.p.A

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Duecoxin

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

6 mg/tablet

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Duecoxin 6 mg chewable tablets for cats

2. Composition

Each chewable tablet contains:

Active substance:
Robenacoxib 6 mg.

Oblong whitish tablet, with one break-mark. The tablet can be divided in two equal parts.

3. Target species

Cats.

4. Indications for use

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

5. Contraindications

Do not use in cats suffering from ulceration in the digestive tract.
Do not use together with other non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids, medicines commonly used in the treatment of pain, inflammation and allergies.
Do not use in cases of hypersensitivity to robenacoxib or to any of the constituents of the tablets.
Do not use in pregnant or lactating cats (see section Special Warnings).

6. Special warnings

Special precautions for safe use in the target species:

The safety of this 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 function of the heart, kidneys or liver or in cats that are dehydrated, have low volume of circulating blood or have low blood pressure may involve additional risk. If use cannot be avoided, these cats require careful monitoring.

Response to long-term 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 at risk of stomach ulcer or if the animal previously displayed intolerance to other NSAIDs.

The 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. 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.

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:

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

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 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 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 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.

Overdose:

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.

7. 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, blood urea nitrogen (BUN) and symmetrical dimethylarginine (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 product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

For oral use.

The recommended dose of robenacoxib is 1 mg/kg body weight with a range 1–2,4 mg/kg. Administer once daily at the same time every day, according to the following table:

Body weight (Kg)	Number of tablets 6 mg
2,5 to 3	½
> 3 to 6	1
> 6 to 9	1 + ½
> 9 to 12	2

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.

9. Advice on correct administration

Give either without food or with small amount of food. The tablets are easy to administer and well accepted by most cats. The tablets can be divided in two equal partsalong the designated score line.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Store below 25 °C.
Keep the blister in the outer carton in order to protect from moisture.
Any unused divided tablet portion should be returned into the blister, kept within the outer carton.

Do not use this veterinary medicinal product after the expiry date which is stated on the blister and the carton after Exp. The expiry date refers to the last day of that month.

Shelf life of halved tablets: 1 day.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Cardboard box with 1 blister (10 chewable tablets)
Cardboard box with 3 blisters (30 chewable tablets)
Cardboard box with 10 blisters (100 chewable tablets)

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
FATRO S.p.A.
Via Emilia, 285
40064, Ozzano dell'Emilia (BO)
Italy

Local representatives and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.