ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior 6 mg tablets for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Robenacoxib 6 mg.

Excipients:

Qualitative composition of excipients and other constituents
Yeast powder
Cellulose, microcrystalline
Povidone (K-30)
Crospovidone
Silica, colloidal anhydrous
Magnesium stearate

Round, beige to brown tablets with imprints “NA” on one side and “AK” 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 in cats.
For the reduction of moderate pain and inflammation associated with orthopaedic surgery in cats.

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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use of the veterinary medicinal product.

In small children, accidental ingestion increases the risk for NSAID adverse effects. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

In pregnant women, particularly near-term pregnant women, prolonged dermal exposure increases the risk for premature closure of the ductus arteriosus in the foetus.

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 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.

Fertility:
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 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

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 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 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 Onsior tablets and Onsior solution for injection has been tested in a target animal safety study and was shown to be well tolerated by cats.

For cats, Onsior 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 are 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 (Onsior 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 Onsior tablets and Onsior solution for injection in 4-month-old cats at overdoses of up to 3 times the maximum recommended dose (2.4 mg, 4.8 mg, 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 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
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} (0.5 h), 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.

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 1.7 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: 4 years.

5.3 Special precautions for storage

Store below 25 °C.

5.4 Nature and composition of immediate packaging

Cardboard box containing 6 x 1, 12 x 1, 30 x 1 or 60 x 1 tablets in Alu/Alu perforated unit dose blisters.
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

Elanco GmbH

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/08/089/001-003
EU/2/08/089/021

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 16/12/2008.

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

{MM/YYYY}

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*).

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior 5 mg tablets for dogs
Onsior 10 mg tablets for dogs
Onsior 20 mg tablets for dogs
Onsior 40 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

5 mg tablets: Robenacoxib 5 mg
10 mg tablets: Robenacoxib 10 mg
20 mg tablets: Robenacoxib 20 mg
40 mg tablets: Robenacoxib 40 mg

Excipients:

Qualitative composition of excipients and other constituents
Yeast powder
Cellulose, microcrystalline
Flavour, artificial beef
Cellulose, powdered
Povidone (K-30)
Crospovidone
Silica, colloidal anhydrous
Magnesium stearate

Round, beige to brown tablets with the imprint "NA" on one side and the following imprint on the other side:

5 mg tablet: AK
10 mg tablet: BE
20 mg tablet: CD
40 mg tablet: BCK

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

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

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 (see section 3.7).

3.4 Special warnings

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 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:
Wash hands after use of the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. In small children, accidental ingestion increases the risk for NSAID adverse effects.

For pregnant women, particularly near-term pregnant women, prolonged dermal exposure increases the risk of premature closure of the ductus arteriosus in the foetus.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Digestive tract disorder[1], Diarrhoea, Vomiting
Common (1 to 10 animals / 100 animals treated):	Elevated liver enzymes[2] Decreased appetite
Uncommon (1 to 10 animals / 1 000 animals treated):	Blood in the 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 increases 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 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.

Fertility:
The safety of the veterinary medicinal product has not been established in dogs 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 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

For oral use.

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.

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

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

Number of tablets by strength and body weight for osteoarthritis

Body weight (kg)	Number of tablets by strength			
	5 mg	10 mg	20 mg	40 mg

2.5 to < 5	1 tablet			
5 to < 10		1 tablet		
10 to < 20			1 tablet	
20 to < 40				1 tablet
40 to 80				2 tablets

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 this 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 2 mg/kg body weight with a range of 2-4 mg/kg. Give as a single oral treatment prior to soft tissue surgery.
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.

Number of tablets by strength and body weight for soft tissue surgery

Body Weight (kg)	**Number of tablets by strength**			
	5 mg	**10 mg**	**20 mg**	**40 mg**
2.5	1 tablet			
> 2.5 to < 5		1 tablet		
5 to < 10			1 tablet	
10 to < 20				1 tablet
20 to < 40				2 tablets
40 to < 60				3 tablets
60 to 80				4 tablets

The interchangeable use of Onsior tablets and Onsior solution for injection has been tested in a target animal safety study and was shown to be well tolerated by dogs.

For dogs, Onsior 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 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.

The interchangeable use of Onsior tablets and Onsior solution for injection in mongrel dogs at overdoses of up to 3 times the maximum recommended dose (2.0, 4.0 and 6.0 plus 4.0, 8.0 and 12.0 mg robenacoxib/kg orally and 2.0 mg, 4.0 mg and 6.0 mg robenacoxib/kg subcutaneously) resulted in dose-related oedema, erythema, thickening of the skin and skin ulceration at the subcutaneous injection site and inflammation, congestion or haemorrhage in the duodenum, jejunum and caecum.

No relevant effects on body weight, bleeding time or evidence of any kidney or liver toxicity were observed.

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

Absorption
After oral administration of robenacoxib flavoured tablets at 1 mg/kg without food, peak blood concentrations are attained rapidly with a T_{max} of 0.5 h, a C_{max} of 1,124 ng/ml and an AUC of 1,249 ng·h/ml. Co-administration of robenacoxib non-flavoured tablets with food produced no delay in T_{max}, but slightly lower values for C_{max} (832 ng/ml) and AUC (782 ng·h/ml). The systemic bioavailability of robenacoxib tablets in dogs was 62% with food and 84% without food.

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

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

Elimination
Robenacoxib is cleared rapidly from blood (CL 0.81 L/kg/h) with an elimination $t_{1/2}$ of 0.7 h after intravenous administration. After oral administration of the tablets, the terminal half-life in blood was

1.2 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 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 4 years.

5.3 Special precautions for storage

Do not store above 25 °C.

5.4 Nature and composition of immediate packaging

Cardboard box containing 7, 14, 28 or 70 tablets in Alu/Alu blisters, 30 x 1 tablets or 60 x 1 tablets in Alu/Alu perforated unit dose blisters.
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

Elanco GmbH

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/08/089/004-019
EU/2/08/089/022-029

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 16/12/2008.

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

{MM/YYYY}

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*).

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior 20 mg/ml solution for injection for cats and dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Robenacoxib 20 mg

Excipients:

Qualitative composition of excipients and other constituents
Sodium metabisulphite (E 223)
Macrogol 400
Ethanol, anhydrous
Poloxamer 188
Citric acid monohydrate
Sodium hydroxide
Water for injections

Clear, colourless to slightly coloured (pink) liquid.

3. CLINICAL INFORMATION

3.1 Target species

Cats and dogs.

3.2 Indications for use for each target species

For the treatment of pain and inflammation associated with orthopaedic or soft tissue surgery in dogs.
For the treatment of pain and inflammation associated with orthopaedic or soft tissue surgery in cats.

3.3 Contraindications

Do not use in animals 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 less than 4 months of age and in dogs less than 2 months of age, or in cats or dogs less than 2.5 kg body weight.

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

Use this veterinary medicinal product under strict veterinary monitoring in cases at risk of gastrointestinal ulceration, or if the animal previously displayed intolerance to other NSAIDs.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands and exposed skin immediately after use of the product.

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

For pregnant women, particularly near-term pregnant women, accidental injection and prolonged dermal exposure increases the risk for premature closure of the ductus arteriosus in the foetus.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cats:

Common (1 to 10 animals / 100 animals treated):	Injection site pain Digestive tract disorder[1], Diarrhoea[1], Vomiting[1]
Uncommon (1 to 10 animals / 1 000 animals treated):	Bloody diarrhoea, Blood in vomit

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

Dogs:

Common (1 to 10 animals / 100 animals treated):	Injection site pain[1] Digestive tract disorder[2], Diarrhoea[2], Vomiting[2]
Uncommon (1 to 10 animals / 1 000 animals treated):	Tarry stool Decreased appetite

[1] Moderate or severe pain at injection site was uncommon.
[2] Most cases were mild and recovered without treatment.

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 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.

Fertility:
The safety of the veterinary medicinal product has not been established in cats and dogs 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 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 or dogs 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 (cats) or urine (dogs) 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

Subcutaneous use.

Administer subcutaneously to cats or dogs approximately 30 minutes before the start of surgery, for example around the time of induction of general anaesthesia, at a dose of 1 ml per 10 kg of body weight (2 mg/kg). After surgery in cats, once daily treatment may be continued at the same dosage and at the same time every day for up to 2 days. After soft tissue surgery in dogs, once daily treatment may be continued at the same dosage and at the same time every day for up to 2 days.

The interchangeable use of Onsior tablets and Onsior solution for injection has been tested in target animal safety studies and was shown to be well tolerated by cats and dogs.

Onsior 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 dogs aged 6 months, once daily subcutaneous administration of robenacoxib at doses of 2 (recommended therapeutic dose; RTD), 6 (3 times RTD), and 20 mg/kg (10 times RTD) for 9 administrations over a 5 week period (3 cycles of 3 consecutive once daily injections) did not produce any signs of toxicity, including gastrointestinal, kidney or liver toxicity and had no effect on bleeding time. Reversible inflammation at the injection site was noted in all groups (including controls) and was more severe in the 6 and 20 mg/kg dose groups.

In healthy young cats aged 10 months, once daily subcutaneous administration of robenacoxib at doses of 4 mg/kg (twice RTD) for 2 consecutive days and 10 mg/kg (5 times RTD) for 3 consecutive days did not produce any signs of toxicity, including signs of gastrointestinal, kidney or liver toxicity and

had no effect on bleeding time. Reversible, minimal injection site reactions were noted in both dose groups.

The interchangeable use of Onsior tablets and Onsior solution for injection in 4-month old cats at overdoses of up to 3 times the maximum recommended dose (2.4 mg, 4.8 mg, 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.

The interchangeable use of Onsior tablets and Onsior solution for injection in mongrel dogs at overdoses of up to 3 times the maximum recommended dose (2.0, 4.0 and 6.0 plus 4.0, 8.0 and 12.0 mg robenacoxib/kg orally and 2.0 mg, 4.0 mg and 6.0 mg robenacoxib/kg subcutaneously) resulted in dose-related oedema, erythema, thickening of the skin and skin ulceration at the subcutaneous injection site and inflammation, congestion, or haemorrhage in the duodenum, jejunum, and caecum. No relevant effects on body weight, bleeding time or evidence of any kidney or liver toxicity were observed.

No changes to blood pressure or the electrocardiogram were observed after single administration to healthy dogs of 2 mg/kg robenacoxib subcutaneously or 2 or 4 mg/kg intravenously. Vomiting occurred 6 or 8 hours post-dosing in 2 of 8 dogs administered the solution for injection at a dosage of 4 mg/kg intravenously.

As with any NSAID, overdose may cause gastrointestinal, kidney, or liver toxicity in sensitive or compromised animals. 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 **cats**, using an *in vitro* whole blood assay, robenacoxib was approximately 500 fold selective for COX-2 (IC_{50} 0.058 μM) as compared to COX-1 (IC_{50} 28.9 μM). *In vivo,* robenacoxib solution for injection produced marked inhibition of COX-2 activity and had no effect on COX-1 activity. At the recommended dosage (2 mg/kg), analgesic, anti-inflammatory and anti-pyretic effects were demonstrated in an inflammation model, and in clinical trials, robenacoxib reduced pain and inflammation in cats undergoing orthopaedic or soft tissue surgery.

In **dogs**, robenacoxib was *in vitro* approximately 140 fold selective for COX-2 (IC_{50} 0.04 μM) as compared to COX-1 (IC_{50} 7.9 μM). *In vivo*, robenacoxib solution for injection produced marked inhibition of COX-2 activity and had no effect on COX-1 activity. At dosages ranging from 0.25 to 4 mg/kg, robenacoxib had analgesic, anti-inflammatory and anti-pyretic effects in an inflammation model with a rapid onset of action (1 h). In clinical trials at the recommended dose (2 mg/kg), robenacoxib reduced pain and inflammation in dogs undergoing orthopaedic or soft tissue surgery, and reduced the need for rescue treatment in dogs undergoing soft tissue surgery.

4.3 Pharmacokinetics

Absorption
Peak blood concentrations of robenacoxib are attained rapidly after subcutaneous injection in cats and dogs. After a dosage of 2 mg/kg a T_{max} of 1 h (cats and dogs), a C_{max} of 1,464 ng/ml (cats) and 615 ng/ml (dogs), and an AUC of 3,128 ng·h/ml (cats) and 2,180 ng·h/ml (dogs) is obtained. After a subcutaneous administration of 1 mg/kg the systemic bioavailability is 69% in cats and 88% in dogs.

Distribution
Robenacoxib has a relatively small volume of distribution (Vss of 190 ml/kg in cats and 240 ml/kg in dogs) and is highly bound to plasma proteins (>99%).

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

Elimination
After intravenous administration robenacoxib was rapidly cleared from blood (CL of 0.44 L/kg/h in cats and 0.81 L/kg/h in dogs) with an elimination $t_{1/2}$ of 1.1 h in cats and 0.8 h in dogs. After subcutaneous administration, the terminal half-life from blood was 1.1 h in cats and 1.2 h in dogs. Robenacoxib persists longer and in higher concentrations at sites of inflammation than in blood. Robenacoxib is excreted predominantly via the biliary route in cats (~70%) and dogs (~65%) and the remainder via the kidneys. Repeated subcutaneous administration at dosages of 2–20 mg/kg produced no change in the blood profile, with neither bioaccumulation of robenacoxib nor enzyme induction. Bioaccumulation of metabolites has not been tested. The pharmacokinetics of robenacoxib injection do not differ between male and female cats and dogs, and are linear over the range of 0.25–4 mg/kg in dogs.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first broaching of the vial: 28 days.

5.3 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C). Refrigeration is not required during the 4-week in-use period after first broaching of the vial. Avoid introduction of contamination. Keep the vial in the outer carton.

5.4 Nature and composition of immediate packaging

Multi-dose amber glass vial containing 20 ml solution for injection, closed with a rubber stopper and sealed with an aluminium cap. One vial packed in a cardboard box.

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

Elanco GmbH

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/08/089/020

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 16/12/2008.

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

{MM/YYYY}

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 II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior 6 mg tablets

2. STATEMENT OF ACTIVE SUBSTANCES

6 mg robenacoxib/tablet

3. PACKAGE SIZE

6 x 1 tablets
12 x 1 tablets
30 x 1 tablets
60 x 1 tablets

4. TARGET SPECIES

Cats.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store below 25 °C.

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

Elanco logo

14. MARKETING AUTHORISATION NUMBERS

EU/2/08/089/001 (6 x 1 tablets)
EU/2/08/089/002 (12 x 1 tablets)
EU/2/08/089/021 (30 x 1 tablets)
EU/2/08/089/003 (60 x 1 tablets)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister foil

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

6 mg

BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior 5 mg tablets
Onsior 10 mg tablets
Onsior 20 mg tablets
Onsior 40 mg tablets

2. STATEMENT OF ACTIVE SUBSTANCES

5 mg robenacoxib/tablet
10 mg robenacoxib/tablet
20 mg robenacoxib/tablet
40 mg robenacoxib/tablet

3. PACKAGE SIZE

7 tablets
14 tablets
28 tablets
70 tablets
30 x 1 tablets
60 x 1 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store below 25 °C.

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

Elanco logo

14. MARKETING AUTHORISATION NUMBERS

Onsior 5 mg tablets for dogs:
EU/2/08/089/004 (7 tablets)
EU/2/08/089/005 (14 tablets)
EU/2/08/089/006 (28 tablets)
EU/2/08/089/007 (70 tablets)
EU/2/08/089/022 (30 x 1 tablets)
EU/2/08/089/023 (60 x 1 tablets)

Onsior 10 mg tablets for dogs:
EU/2/08/089/008 (7 tablets)
EU/2/08/089/009 (14 tablets)
EU/2/08/089/010 (28 tablets)
EU/2/08/089/011 (70 tablets)
EU/2/08/089/024 (30 x 1 tablets)
EU/2/08/089/025 (60 x 1 tablets)

Onsior 20 mg tablets for dogs:
EU/2/08/089/012 (7 tablets)
EU/2/08/089/013 (14 tablets)
EU/2/08/089/014 (28 tablets)
EU/2/08/089/015 (70 tablets)
EU/2/08/089/026 (30 x 1 tablets)
EU/2/08/089/027 (60 x 1 tablets)

Onsior 40 mg tablets for dogs:
EU/2/08/089/016 (7 tablets)
EU/2/08/089/017 (14 tablets)
EU/2/08/089/018 (28 tablets)
EU/2/08/089/019 (70 tablets)
EU/2/08/089/028 (30 x 1 tablets)

EU/2/08/089/029 (60 x 1 tablets)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister foil

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

5 mg
10 mg
20 mg
40 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior 20 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

20 mg/ml robenacoxib

3. PACKAGE SIZE

20 ml

4. TARGET SPECIES

Cats and dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator (2 °C – 8 °C). Keep the vial in the outer carton.
Refrigeration is not required during the 4-week in-use period after first broaching of the vial.

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

Elanco logo

14. MARKETING AUTHORISATION NUMBERS

EU/2/08/089/020

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Glass vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Onsior

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

20 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Onsior 6 mg tablets for cats

2. Composition

Each tablet contains 6 mg robenacoxib.

Round, beige to brown, non-divisible tablets with imprints “NA” on one side and “AK” on the other side.

3. Target species

Cats.

4. Indications for use

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

5. Contraindications

Do not use in cats suffering from ulceration in the digestive tract.
Do not use together with non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids, medicines commonly used in the treatment of pain, inflammation and allergies.
Do not use in case of hypersensitivity to robenacoxib or to any of the constituents of the tablets.
Do not use in pregnant or lactating cats or cats used for breeding because the safety of this product has not been established in these animals.

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 risks. 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use of the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. In small children, accidental ingestion increases the risk for NSAID adverse effects.
For pregnant women, particularly near term pregnant women, prolonged dermal exposure may increase the risk to the foetus.

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

Fertility:
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 glucocorticosteroids. 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 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.

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.

The interchangeable use of Onsior tablets and Onsior solution for injection in 4-month old cats at overdoses of up to 3 times the maximum recommended dose (2.4 mg, 4.8 mg, 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 a 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.

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, 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 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 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. 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.

The interchangeable use of Onsior tablets and Onsior solution for injection has been tested in a target animal safety study and was shown to be well tolerated by the cats.

For cats, Onsior solution for injection or tablets may be used interchangeably in accordance with the indications and duration 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 are different.

9. Advice on correct administration

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 should not be divided or broken.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 25 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton or blister after Exp. The expiry date refers to the last day of that month.

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

EU/2/08/089/001-003; EU/2/08/089/021

Cardboard boxes containing 6 x 1, 12 x 1, 30 x 1 or 60 x 1 tablets in Alu/Alu perforated unit dose blisters. Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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 contact details to report suspected adverse reactions:
Elanco GmbH, Heinz-Lohmann-Str. 4, 27472 Cuxhaven, Germany

België/Belgique/Belgien:
PV.BEL@elancoah.com
+3233000338

Република България:
PV.BGR@elancoah.com
+48221047815

Česká republika:
PV.CZE@elancoah.com
+420228880231

Danmark:
PV.DNK@elancoah.com
+4578775477

Deutschland:
PV.DEU@elancoah.com
+4932221852372

Eesti:
PV.EST@elancoah.com
+ 3728807513

Ελλάδα:
PV.GRC@elancoah.com
+38682880137

España:
PV.ESP@elancoah.com
+34518890402

France:
PV.FRA@elancoah.com
+33975180507

Hrvatska:
PV.HRV@elancoah.com
+3618088411

Ireland:
PV.IRL@elancoah.com
+443308221732

Ísland:

Lietuva:
PV.LTU@elancoah.com
+3728840390

Luxembourg/Luxemburg:
PV.LUX@elancoah.com
+35220881943

Magyarország:
PV.HUN@elancoah.com
+3618506968

Malta:
PV.MLT@elancoah.com
+3618088530

Nederland:
PV.NLD@elancoah.com
+31852084939

Norge:
PV.NOR@elancoah.com
+4781503047

Österreich:
PV.AUT@elancoah.com
+43720116570

Polska:
PV.POL@elancoah.com
+48221047306

Portugal:
PV.PRT@elancoah.com
+351308801355

România:
PV.ROU@elancoah.com
+40376300400

Slovenija:
PV.SVN@elancoah.com
+38682880093

Slovenská republika:

PV.ISL@elancoah.com
+4589875379

Italia:
PV.ITA@elancoah.com
+390282944231

Κύπρος:
PV.CYP@elancoah.com
+38682880096

Latvija:
PV.LVA@elancoah.com
+3728840390

PV.SVK@elancoah.com
+420228880231

Suomi/Finland:
PV.FIN@elancoah.com
+358753252088

Sverige:
PV.SWE@elancoah.com
+46108989397

United Kingdom (Northern Ireland):
PV.XXI@elancoah.com
+443308221732

Manufacturer responsible for batch release:
Elanco France S.A.S., 26 Rue de la Chapelle, 68330 Huningue, France

17. Other information

Robenacoxib is a non-steroidal anti-inflammatory drug (NSAID). It selectively inhibits the cyclooxygenase 2 enzyme (COX-2), which is responsible for pain, inflammation or fever. The cyclooxygenase 1 enzyme (COX-1) which has protective functions, e.g. in the digestive tract and kidneys, is not inhibited by robenacoxib. In clinical trials in cats this product 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.

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Onsior 5 mg tablets for dogs
Onsior 10 mg tablets for dogs
Onsior 20 mg tablets for dogs
Onsior 40 mg tablets for dogs

2. Composition

Each tablet contains:

Robenacoxib	Imprints
5 mg	AK
10 mg	BE
20 mg	CD
40 mg	BCK

Round, beige to brown, non-divisible tablets with the imprint "NA" on one side and the upper-mentioned imprint on the other side.

3. Target species

Dogs.

4. Indications for use

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

5. Contraindications

Do not use in dogs suffering from stomach ulcer or with liver disease.
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 case of hypersensitivity to robenacoxib or to any of the ingredients of the tablets.
Do not use in pregnant or lactating bitches because the safety of robenacoxib has not been established during pregnancy and lactation or in dogs used for breeding.

6. Special warnings

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

Special precautions for safe use in the target species:
The safety of this 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 symptoms such as anorexia, apathy or vomiting in combination with elevated liver enzymes.

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

Use this veterinary medicinal product under strict veterinary monitoring in dogs at risk of stomach ulcer or if the animal previously displayed intolerance to other NSAIDs.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use of the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. In small children, accidental ingestion increases the risk for NSAID adverse effects.

For pregnant women, particularly near-term pregnant women, prolonged dermal exposure might increase the risk to the foetus.

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

Fertility:
The safety of the veterinary medicinal product has not been established in dogs 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 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.

Overdose:
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.

The interchangeable use of Onsior tablets and Onsior solution for injection in mongrel dogs at overdoses of up to 3 times the maximum recommended dose (2.0, 4.0 and 6.0 plus 4.0, 8.0 and 12.0 mg robenacoxib/kg orally and 2.0 mg, 4.0 mg and 6.0 mg robenacoxib/kg subcutaneously) resulted in dose-related oedema, erythema, thickening of the skin and skin ulceration at the subcutaneous injection site and inflammation, congestion or haemorrhage in the duodenum, jejunum and caecum. No relevant effects on body weight, bleeding time or evidence of any kidney or liver toxicity were observed.

7. Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Digestive tract disorder[1], Diarrhoea, Vomiting
Common (1 to 10 animals / 100 animals treated):	Elevated liver enzymes[2] Decreased appetite
Uncommon (1 to 10 animals / 1 000 animals treated):	Blood in the 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 increases 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 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 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.

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

Number of tablets by strength and body weight for osteoarthritis

Body weight (kg)	**Number of tablets by strength**			
	5 mg	**10 mg**	**20 mg**	**40 mg**
2.5 to < 5	1 tablet			
5 to < 10		1 tablet		
10 to < 20			1 tablet	
20 to < 40				1 tablet
40 to 80				2 tablets

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 this 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 2 mg/kg body weight with a range of 2-4 mg/kg. Give as a single oral treatment prior to soft tissue surgery.
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.

Number of tablets by strength and body weight for soft tissue surgery

Body weight (kg)	**Number of tablets by strength**			
	5 mg	**10 mg**	**20 mg**	**40 mg**
2.5	1 tablet			
> 2.5 to < 5		1 tablet		
5 to < 10			1 tablet	
10 to < 20				1 tablet
20 to < 40				2 tablets
40 to < 60				3 tablets
60 to 80				4 tablets

The interchangeable use of Onsior tablets and Onsior solution for injection has been tested in a target animal safety study and was shown to be well tolerated by dogs.

For dogs, Onsior 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.

9. Advice on correct administration

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. Soft Tissue Surgery: Administer the first dose at least 30 minutes prior to surgery. The tablets are flavoured and are taken voluntarily by most dogs. The tablets should not be divided or broken.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 25 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton or blister after Exp. The expiry date refers to the last day of that month.

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

EU/2/08/089/004-019; EU/2/08/089/022-029

Cardboard boxes containing 7, 14, 28 or 70 tablets in Alu/Alu blisters, 30 x 1 tablets or 60 x 1 tablets in Alu/Alu perforated unit dose blisters. Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Elanco GmbH, Heinz-Lohmann-Str. 4, 27472 Cuxhaven, Germany

België/Belgique/Belgien:
PV.BEL@elancoah.com
+3233000338

Република България:
PV.BGR@elancoah.com
+48221047815

Česká republika:
PV.CZE@elancoah.com
+420228880231

Danmark:
PV.DNK@elancoah.com
+4578775477

Deutschland:
PV.DEU@elancoah.com
+4932221852372

Lietuva:
PV.LTU@elancoah.com
+3728840390

Luxembourg/Luxemburg:
PV.LUX@elancoah.com
+35220881943

Magyarország:
PV.HUN@elancoah.com
+3618506968

Malta:
PV.MLT@elancoah.com
+3618088530

Nederland:
PV.NLD@elancoah.com
+31852084939

Eesti:
PV.EST@elancoah.com
+ 3728807513

Ελλάδα:
PV.GRC@elancoah.com
+38682880137

España:
PV.ESP@elancoah.com
+34518890402

France:
PV.FRA@elancoah.com
+33975180507

Hrvatska:
PV.HRV@elancoah.com
+3618088411

Ireland:
PV.IRL@elancoah.com
+443308221732

Ísland:
PV.ISL@elancoah.com
+4589875379

Italia:
PV.ITA@elancoah.com
+390282944231

Κύπρος:
PV.CYP@elancoah.com
+38682880096

Latvija:
PV.LVA@elancoah.com
+3728840390

Norge:
PV.NOR@elancoah.com
+4781503047

Österreich:
PV.AUT@elancoah.com
+43720116570

Polska:
PV.POL@elancoah.com
+48221047306

Portugal:
PV.PRT@elancoah.com
+351308801355

România:
PV.ROU@elancoah.com
+40376300400

Slovenija:
PV.SVN@elancoah.com
+38682880093

Slovenská republika:
PV.SVK@elancoah.com
+420228880231

Suomi/Finland:
PV.FIN@elancoah.com
+358753252088

Sverige:
PV.SWE@elancoah.com
+46108989397

United Kingdom (Northern Ireland):
PV.XXI@elancoah.com
+443308221732

Manufacturer responsible for batch release:
Elanco France S.A.S., 26 Rue de la Chapelle, 68330 Huningue, France

17. Other information

Robenacoxib is a non-steroidal anti-inflammatory drug (NSAID). It selectively inhibits the cyclooxygenase 2 enzyme (COX-2), which is responsible for pain, inflammation or fever. The cyclooxygenase 1 enzyme (COX-1) which has protective functions, e.g. in the digestive tract and kidneys, is not inhibited by robenacoxib.
In artificially induced inflammation in dogs, robenacoxib reduced pain and inflammation with single oral doses ranging from 0.5 to 8 mg/kg and a rapid onset of action (0.5 h). In clinical trials this product reduced the lameness and inflammation of dogs with chronic osteoarthritis and pain, inflammation and the need for rescue treatment in dogs undergoing soft tissue surgery.

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Onsior 20 mg/ml solution for injection for cats and dogs

2. Composition

Each ml contains 20 mg robenacoxib as active substance and 1 mg sodium metabisulphite (E 223) as an antioxidant.

Clear, colourless to slightly coloured (pink) liquid.

3. Target species

Cats and dogs.

4. Indications for use

For the treatment of pain and inflammation associated with orthopaedic or soft tissue surgery in dogs.
For the treatment of pain and inflammation associated with orthopaedic or soft tissue surgery in cats.

5. Contraindications

Do not use in animals suffering from gastrointestinal ulceration.
Do not use together with corticosteroids or other non-steroidal anti-inflammatory drugs (NSAIDs).
Do not use in case of hypersensitivity to robenacoxib or to any ingredients of the solution.
Do not use in pregnant or lactating animals because the safety of robenacoxib has not been established during pregnancy and lactation or in cats and dogs used for breeding.

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 less than 4 months of age and in dogs less than 2 months of age, or in cats or dogs less than 2.5 kg body weight.
Use in animals with impaired function of the heart, kidneys or liver or in animals that are dehydrated, have low volume of circulating blood or have low blood pressure may involve additional risks. If use cannot be avoided, these animals require careful monitoring and fluid therapy.

Use this veterinary medicinal product under strict veterinary monitoring in animals at risk of ulceration of the digestive tract, or if the animal previously displayed intolerance to other NSAIDs.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands and exposed skin immediately after use of the veterinary medicinal product.

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

For pregnant women, particularly near term pregnant women, accidental injection and prolonged dermal exposure might increase the risk to the foetus.

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 or dogs 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 (cats) or urine (dogs) 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.

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

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

Overdose:
In healthy young dogs aged 6 months, once daily subcutaneous administration of robenacoxib at doses of 2 (recommended therapeutic dose; RTD), 6 (3 times RTD), and 20 mg/kg (10 times RTD) for 9 administrations over a 5 week period (3 cycles of 3 consecutive once daily injections) did not produce any signs of toxicity, including gastrointestinal, kidney or liver toxicity and had no effect on bleeding time. Reversible inflammation at the injection site was noted in all groups (including controls) and was more severe in the 6 and 20 mg/kg dose groups.

In healthy young cats aged 10 months, once daily subcutaneous administration of robenacoxib at doses of 4 mg/kg (twice RTD) for 2 consecutive days and 10 mg/kg (5 times RTD) for 3 consecutive days did not produce any signs of toxicity, including signs of gastrointestinal, kidney or liver toxicity and had no effect on bleeding time. Reversible, minimal injection site reactions were noted in both dose groups.

The interchangeable use of Onsior tablets and Onsior solution for injection in 4-month old cats at overdoses of up to 3 times the maximum recommended dose (2.4 mg, 4.8 mg, 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 a single intravenous administration of 2 or 4 mg/kg robenacoxib to anaesthetised healthy cats.

The interchangeable use of Onsior tablets and Onsior solution for injection in mongrel dogs at overdoses of up to 3 times the maximum recommended dose (2.0, 4.0 and 6.0 plus 4.0, 8.0 and 12.0 mg robenacoxib/kg orally and 2.0 mg, 4.0 mg and 6.0 mg robenacoxib/kg subcutaneously) resulted in dose-related oedema, erythema, thickening of the skin and skin ulceration at the subcutaneous injection site and inflammation, congestion, or haemorrhage in the duodenum, jejunum, and caecum. No relevant effects on body weight, bleeding time or evidence of any kidney or liver toxicity were observed.

No changes to blood pressure or the electrocardiogram were observed after single administration to healthy dogs of 2 mg/kg robenacoxib subcutaneously or 2 or 4 mg/kg intravenously. Vomiting occurred 6 or 8 hours post-dosing in 2 of 8 dogs administered the solution for injection at a dosage of 4 mg/kg intravenously.

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

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Cats:

Common (1 to 10 animals / 100 animals treated):	Injection site pain Digestive tract disorder[1], Diarrhoea[1], Vomiting[1]
Uncommon (1 to 10 animals / 1 000 animals treated):	Bloody diarrhoea, Blood in vomit

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

Dogs:

Common (1 to 10 animals / 100 animals treated):	Injection site pain[1] Digestive tract disorder[2], Diarrhoea[2], Vomiting[2]
Uncommon (1 to 10 animals / 1 000 animals treated):	Tarry stool Decreased appetite

[1]Moderate or severe pain at injection site was uncommon.
[2]Most cases were mild and recovered without treatment.

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 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

Subcutaneous use.

Administer the solution subcutaneously to cats or dogs approximately 30 minutes before the start of surgery, for example around the time of induction of general anaesthesia, at a dose of 1 ml per 10 kg of body weight (2 mg/kg). After surgery in cats, once daily treatment may be continued at the same dosage and at the same time every day for up to 2 days. After soft tissue surgery in dogs, once daily treatment may be continued at the same dosage and at the same time every day for up to 2 days.

The interchangeable use of Onsior tablets and Onsior solution for injection has been tested in target animal safety studies and was shown to be well tolerated by cats and dogs.

Onsior solution for injection or tablets may be used interchangeably in accordance with the indications and duration of use approved for each pharmaceutical form. Treatment should not exceed one dose (either tablet or injection) per day. Please note that recommended doses for the two formulations may be different.

9. Advice on correct administration

None.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store in a refrigerator (2 °C – 8 °C).
Avoid introduction of contamination. Keep the vial in the outer carton.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton or bottle after Exp. The expiry date refers to the last day of that month.
After first broaching of the vial, the product may be stored for 28 days.
Refrigeration is not required during the 4-week in-use period after first broaching of the vial.

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

EU/2/08/089/020
Cardboard box containing 1 vial with 20 ml solution for injection.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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 contact details to report suspected adverse reactions:
Elanco GmbH, Heinz-Lohmann-Str. 4, 27472 Cuxhaven, Germany

België/Belgique/Belgien:
PV.BEL@elancoah.com
+3233000338

Република България:
PV.BGR@elancoah.com
+48221047815

Česká republika:
PV.CZE@elancoah.com
+420228880231

Danmark:
PV.DNK@elancoah.com
+4578775477

Deutschland:
PV.DEU@elancoah.com
+4932221852372

Eesti:
PV.EST@elancoah.com
+ 3728807513

Ελλάδα:
PV.GRC@elancoah.com
+38682880137

España:
PV.ESP@elancoah.com
+34518890402

France:
PV.FRA@elancoah.com
+33975180507

Hrvatska:
PV.HRV@elancoah.com

Lietuva:
PV.LTU@elancoah.com
+3728840390

Luxembourg/Luxemburg:
PV.LUX@elancoah.com
+35220881943

Magyarország:
PV.HUN@elancoah.com
+3618506968

Malta:
PV.MLT@elancoah.com
+3618088530

Nederland:
PV.NLD@elancoah.com
+31852084939

Norge:
PV.NOR@elancoah.com
+4781503047

Österreich:
PV.AUT@elancoah.com
+43720116570

Polska:
PV.POL@elancoah.com
+48221047306

Portugal:
PV.PRT@elancoah.com
+351308801355

România:
PV.ROU@elancoah.com

+3618088411

Ireland:
PV.IRL@elancoah.com
+443308221732

Ísland:
PV.ISL@elancoah.com
+4589875379

Italia:
PV.ITA@elancoah.com
+390282944231

Κύπρος:
PV.CYP@elancoah.com
+38682880096

Latvija:
PV.LVA@elancoah.com
+3728840390

+40376300400

Slovenija:
PV.SVN@elancoah.com
+38682880093

Slovenská republika:
PV.SVK@elancoah.com
+420228880231

Suomi/Finland:
PV.FIN@elancoah.com
+358753252088

Sverige:
PV.SWE@elancoah.com
+46108989397

United Kingdom (Northern Ireland):
PV.XXI@elancoah.com
+443308221732

Manufacturer responsible for batch release:
Elanco France S.A.S., 26 Rue de la Chapelle, 68330 Huningue, France

17. Other information

Robenacoxib is a non-steroidal anti-inflammatory drug (NSAID). It selectively inhibits the cyclooxygenase 2 enzyme (COX-2), which is responsible for pain, inflammation or fever. The cyclooxygenase 1 enzyme (COX-1) which has protective functions, e.g. in the digestive tract and kidneys, is not inhibited by robenacoxib.
In artificially induced inflammation in cats and dogs, robenacoxib reduced pain, inflammation and fever at the recommended doses with a rapid onset of action (1 h). In clinical trials this product reduced pain and inflammation in cats and dogs undergoing orthopaedic or soft tissue surgery, and reduced the need for rescue treatment in dogs undergoing soft tissue surgery.