

**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.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Tablet.

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

## **4. CLINICAL PARTICULARS**

### **4.1 Target species**

Cats.

### **4.2 Indications for use, specifying the 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.

### **4.3 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 4.7).

### **4.4 Special warnings for each target species**

None.

### **4.5 Special precautions for use**

#### Special precautions for use in animals

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

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

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

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

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

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.

#### **4.6 Adverse reactions (frequency and seriousness)**

Mild and transient diarrhoea, soft faeces or vomiting were commonly reported in clinical trials with treatment up to 6 days. Lethargy may be observed in very rare cases. In addition, elevated renal parameters (creatinine, BUN and SDMA), and renal insufficiency have been reported very rarely in post marketing safety experience, more commonly in older cats and with concomitant use of anaesthetic or sedative agents (see also Sections 4.5 Special precautions for use, 4.8 Interaction with other medicinal products and forms of interaction, and 4.9 Amounts to be administered and administration route).

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

#### **4.7 Use during pregnancy, lactation or lay**

Do not use in pregnant and lactating animals because the safety of robenacoxib has not been established during pregnancy and lactation or in cats used for breeding.

#### **4.8 Interaction with other medicinal products and other forms of interaction**

Onsior 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 Onsior. 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 Onsior 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.

#### 4.9 Amounts to be administered and administration route

For oral use.

Give either without food or with a small amount of food. Onsior 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 4.5.

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.

#### 4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

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.

#### **4.11 Withdrawal period(s)**

Not applicable.

## **5. PHARMACOLOGICAL PROPERTIES**

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids, coxibs.  
ATCvet code: QM01AH91.

### **5.1 Pharmacodynamic properties**

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<sub>2</sub> 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<sub>50</sub> 0.058 µM) as compared to COX-1 (IC<sub>50</sub> 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.

### **5.2 Pharmacokinetic particulars**

#### Absorption

After oral administration of robenacoxib tablets at approximately 2 mg/kg without food, peak blood concentrations are attained rapidly with a T<sub>max</sub> of 0.5 h, a C<sub>max</sub> 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 ( $V_{ss}$  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.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Yeast powder  
Cellulose, microcrystalline  
Povidone (K-30)  
Crospovidone  
Silica, colloidal anhydrous  
Magnesium stearate

### **6.2 Major incompatibilities**

Not applicable.

### **6.3 Shelf life**

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

### **6.4 Special precautions for storage**

Store below 25 °C.

### **6.5 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.

### **6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products**

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## **7. MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

## **8.     MARKETING AUTHORISATION NUMBERS**

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

## **9.     DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 16/12/2008.  
Date of last renewal: 08/11/2013.

## **10    DATE OF REVISION OF THE TEXT**

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

## **PROHIBITION OF SALE, SUPPLY AND/OR USE**

Not applicable.

## 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

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Tablet

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

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Dogs.

### 4.2 Indications for use, specifying the 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.

### 4.3 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 4.7).

### 4.4 Special warnings for each target species

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



## **4.5 Special precautions for use**

### Special precautions for use in animals

The safety of the veterinary medicinal product has not been established in dogs weighing less than 2.5 kg or under 3 months of age.

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

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

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

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

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.

## **4.6 Adverse reactions (frequency and seriousness)**

Gastrointestinal adverse events were reported very commonly, but most cases were mild and recovered without treatment. Vomiting and soft faeces were very common, decreased appetite and diarrhoea were common, and blood in the faeces was uncommon.

In dogs treated up to 2 weeks no increases in liver enzyme activities were observed. However, with long-term treatment, increases in liver enzyme activities were common. 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. In very rare cases, lethargy may be observed.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

## **4.7 Use during pregnancy, lactation or lay**

Do not use in pregnant or lactating dogs because the safety of robenacoxib has not been established during pregnancy and lactation or in dogs used for breeding.

#### 4.8 Interaction with other medicinal products and other forms of interaction

Onsior 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 Onsior. 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 Onsior 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.

#### 4.9 Amounts to be administered and administration route

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.

Onsior 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 Onsior 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.

### 4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

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.

### 4.11 Withdrawal period(s)

Not applicable.

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory and anti-rheumatic products, non-steroids, coxibs.  
ATCvet code: QM01AH91.

### 5.1 Pharmacodynamic properties

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<sub>2</sub> 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<sub>50</sub> 0.04 µM) as compared to COX-1 (IC<sub>50</sub> 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<sub>50</sub> 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.

## 5.2 Pharmacokinetic particulars

### Absorption

After oral administration of robenacoxib flavoured tablets at 1 mg/kg without food, peak blood concentrations are attained rapidly with a T<sub>max</sub> of 0.5 h, a C<sub>max</sub> 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<sub>max</sub>, but slightly lower values for C<sub>max</sub> (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 (V<sub>ss</sub> 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<sub>1/2</sub> 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.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Yeast powder  
Cellulose, microcrystalline  
Flavour, artificial beef  
Cellulose, powdered  
Povidone (K-30)  
Crospovidone  
Silica, colloidal anhydrous  
Magnesium stearate

### 6.2 Major incompatibilities

Not applicable.

### 6.3 Shelf life

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

#### **6.4. Special precautions for storage**

Do not store above 25 °C.

#### **6.5 Nature and composition of immediate packaging**

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

Not all pack sizes may be marketed.

#### **6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products**

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

### **7. MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

### **8. MARKETING AUTHORISATION NUMBER(S)**

EU/2/08/089/004-019

EU/2/08/089/022-029

### **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 16/12/2008.

Date of last renewal: 08/11/2013.

### **10 DATE OF REVISION OF THE TEXT**

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

### **PROHIBITION OF SALE, SUPPLY AND/OR USE**

Not applicable.

## 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

### Excipient:

Sodium metabisulphite (E 223)

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless to slightly coloured (pink) liquid.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Cats and dogs.

### 4.2 Indications for use, specifying the 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.

### 4.3 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 4.7).

### 4.4 Special warnings for each target species

None.

### 4.5 Special precautions for use

#### Special precautions for use in animals

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.

#### **4.6 Adverse reactions (frequency and seriousness)**

Cats:

Gastrointestinal adverse events (vomiting, soft faeces or diarrhoea) were commonly reported, but most cases were mild and recovered without treatment. Diarrhoea or vomiting with blood were uncommon. Pain at injection site was commonly reported.

Dogs:

Gastrointestinal adverse events (diarrhoea and vomiting) were commonly reported but most cases were mild and recovered without treatment. Soft and dark faeces or reduced appetite were uncommon. Slight pain at injection site was commonly reported. Moderate or severe pain at injection site was uncommon.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

#### **4.7 Use during pregnancy, lactation or lay**

Do not use in pregnant and lactating animals because the safety of robenacoxib has not been established during pregnancy and lactation or in cats and dogs used for breeding.

#### **4.8 Interaction with other medicinal products and other forms of interaction**

Onsior 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 Onsior. 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 Onsior 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.

#### **4.9 Amounts to be administered and administration route**

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.

#### **4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary**

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.

#### **4.11 Withdrawal period(s)**

Not applicable.

## **5. PHARMACOLOGICAL PROPERTIES**

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, coxibs.  
ATCvet code: QM01AH91.

### **5.1 Pharmacodynamic properties**

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<sub>2</sub> 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<sub>50</sub> 0.058 µM) as compared to COX-1 (IC<sub>50</sub> 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<sub>50</sub> 0.04 µM) as compared to COX-1 (IC<sub>50</sub> 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.

### **5.2 Pharmacokinetic particulars**

#### 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<sub>max</sub> of 1 h (cats and dogs), a C<sub>max</sub> 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 (V<sub>ss</sub> 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.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Macrogol 400  
Ethanol, anhydrous  
Poloxamer 188  
Citric acid monohydrate  
Sodium metabisulphite (E 223)  
Sodium hydroxide  
Water for injections

### **6.2 Major incompatibilities**

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

### **6.3 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.

### **6.4 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.

### **6.5 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.

### **6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products**

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## **7. MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

**8. MARKETING AUTHORISATION NUMBER(S)**

EU/2/08/089/020

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 16/12/2008.

Date of last renewal: 08/11/2013.

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

**PROHIBITION OF SALE, SUPPLY AND/OR USE**

Not applicable.

**ANNEX II**

- A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY OR USE**
- C. STATEMENT OF THE MRLs**

**A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturers responsible for batch release

*Tablets:*

Elanco France S.A.S  
26 Rue de la Chapelle  
68330 Huningue  
FRANCE

*Solution for injection:*

Elanco France S.A.S  
26 Rue de la Chapelle  
68330 Huningue  
FRANCE

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY OR USE**

Veterinary medicinal product subject to prescription.

**C. STATEMENT OF THE MRLs**

Not applicable.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**NATURE/TYPE:** Cardboard box

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Onsior 6 mg tablets for cats  
Robenacoxib

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each tablet contains 6 mg Robenacoxib

**3. PHARMACEUTICAL FORM**

Tablet

**4. PACKAGE SIZE**

6 x1 tablets  
12 x 1 tablets  
30 x 1 tablets  
60 x 1 tablets

**5. TARGET SPECIES**

Cats

**6. INDICATION(S)**

Not applicable.

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use. Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Not applicable.

**9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.



**10. EXPIRY DATE**

EXP {month/year}

**11. SPECIAL STORAGE CONDITIONS**

Store below 25 °C.

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

Disposal: read package leaflet.

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

**16. MARKETING AUTHORISATION NUMBER(S)**

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)

**17. MANUFACTURER'S BATCH NUMBER**

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**NATURE/TYPE: Blister foil**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Onsior 6 mg  
Robenacoxib



**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Elanco

**3. EXPIRY DATE**

EXP {month/year}

**4. BATCH NUMBER**

Lot {number}

**5. THE WORDS “FOR ANIMAL TREATMENT ONLY”**

For animal treatment only.

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**NATURE/TYPE:** Cardboard box

**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  
Robenacoxib

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each tablet contains 5 mg Robenacoxib  
Each tablet contains 10 mg Robenacoxib  
Each tablet contains 20 mg Robenacoxib  
Each tablet contains 40 mg Robenacoxib

**3. PHARMACEUTICAL FORM**

Tablet

**4. PACKAGE SIZE**

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

**5. TARGET SPECIES**

Dogs

**6. INDICATION(S)**

Not applicable

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use. Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Not applicable.

**9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}

**11. SPECIAL STORAGE CONDITIONS**

Store below 25 °C.

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

Disposal: read package leaflet.

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

**16. MARKETING AUTHORISATION NUMBER(S)**

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)

<b>17. MANUFACTURER'S BATCH NUMBER</b>
--

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**NATURE/TYPE: Blister foil**

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Onsior 5 mg  
Onsior 10 mg  
Onsior 20 mg  
Onsior 40 mg  
Robenacoxib



**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Elanco

**3. EXPIRY DATE**

EXP {month/year}

**4. BATCH NUMBER**

Lot {number}

**5. THE WORDS “FOR ANIMAL TREATMENT ONLY”**

For animal treatment only.

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**NATURE/TYPE:** Cardboard box

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

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

**2. STATEMENT OF ACTIVE SUBSTANCES**

20 mg/ml Robenacoxib

**3. PHARMACEUTICAL FORM**

Solution for injection

**4. PACKAGE SIZE**

20 ml

**5. TARGET SPECIES**

Cats and dogs

**6. INDICATION(S)**

Not applicable.

**7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Subcutaneous use. Read the package leaflet before use.

**8. WITHDRAWAL PERIOD(S)**

Not applicable.

**9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}  
Once broached, use within 28 days by ...

**11. SPECIAL STORAGE CONDITIONS**

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.

**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**

Disposal: read package leaflet.

**13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE**

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

**16. MARKETING AUTHORISATION NUMBER(S)**

EU/2/08/089/020

**17. MANUFACTURER’S BATCH NUMBER**

Lot {number}



**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**NATURE/TYPE:** Glass vial

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

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

**2. QUANTITY OF THE ACTIVE SUBSTANCE(S)**

20 mg/ml

**3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES**

20 ml

**4. ROUTE(S) OF ADMINISTRATION**

SC

**5. WITHDRAWAL PERIOD(S)**

Not applicable

**6. BATCH NUMBER**

Lot {number}

**7. EXPIRY DATE**

EXP {month/year}  
Once broached, use by ...

**8. THE WORDS "FOR ANIMAL TREATMENT ONLY"**

For animal treatment only.

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET:  
Onsior 6 mg tablets for cats**

**1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Marketing authorisation holder:

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

Manufacturer responsible for the batch release:

Elanco France S.A.S  
26 Rue de la Chapelle  
68330 Huningue  
FRANCE

**2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Onsior 6 mg tablets for cats  
Robenacoxib

**3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)**

Each tablet contains 6 mg robenacoxib.

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

Onsior tablets are easy to administer and well accepted by most cats.

**4. INDICATION(S)**

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. ADVERSE REACTIONS**

Mild and transient diarrhoea, soft faeces or vomiting were commonly reported in clinical trials with treatment up to 6 days. Lethargy may be observed in very rare cases. In addition, elevated renal parameters (creatinine, BUN and SDMA), and renal insufficiency have been reported very rarely in post marketing safety experience, more commonly in older cats and with concomitant use of anaesthetic or

sedative agents (see also Sections: Special precautions for use, Interaction with other medicinal products and forms of interaction, and dosage for each species, route(s) and method of administration).

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

## **7. TARGET SPECIES**

Cats.

## **8. DOSAGE FOR EACH SPECIES, ROUTE(S) 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.

<b>Body weight (kg)</b>	<b>Number of tablets</b>
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. Onsior tablets are easy to administer and well accepted by most cats. The tablets should not be divided or broken.

## **10. WITHDRAWAL PERIOD(S)**

Not applicable.

## **11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children. Store below 25 °C. Do not use after the expiry date stated on the label or blister after EXP.

## **12. SPECIAL WARNING(S)**

### Special precautions for use in animals:

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:

Do not use in pregnant and lactating animals because the safety of robenacoxib has not been established during pregnancy and lactation or in cats used for breeding.

### Interaction with other medicinal products and other forms of interaction:

Onsior 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 Onsior. 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 Onsior 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 (symptoms, emergency procedures, 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.

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.

**13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY**

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

**14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

Detailed information on this product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

**15. OTHER INFORMATION**

Onsior tablets for cats are available in 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.

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.

For any information about this veterinary medicinal product, please contact the marketing authorisation holder.

**PACKAGE LEAFLET:**  
**Onsior 5 mg tablets for dogs**  
**Onsior 10 mg tablets for dogs**  
**Onsior 20 mg tablets for dogs**  
**Onsior 40 mg tablets for dogs**

**1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Marketing authorisation holder:

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

Manufacturer responsible for the batch release:

Elanco France S.A.S  
26 Rue de la Chapelle  
68330 Huningue  
FRANCE

**2. 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  
Robenacoxib

**3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)**

Each tablet contains the following amount of robenacoxib and bears the imprint “NA” on one side and the following imprint on the other side:

<u>Robenacoxib/tablet</u>	<u>Imprints</u>
5 mg	AK
10 mg	BE
20 mg	CD
40 mg	BCK

Tablets are round, beige to brown and non-divisible. Onsior tablets are flavoured and are taken voluntarily by most dogs.

**4. INDICATION(S)**

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. ADVERSE REACTIONS

Adverse reactions of the digestive tract were reported very commonly, but most cases were mild and recovered without treatment. Vomiting and soft faeces were very common, decreased appetite and diarrhoea were common, and blood in the faeces was uncommon.

In dogs treated up to 2 weeks no increases in liver enzyme activities were observed. However, with long-term treatment increases in liver enzyme activities were common. In most cases the liver enzyme activities either stabilised or decreased with continued treatment. Increases in liver enzyme activities associated with symptoms of anorexia, apathy or vomiting were uncommon. In very rare cases, lethargy may be observed.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

## 7. TARGET SPECIES

Dogs.

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

**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 Onsior 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**

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

**10. WITHDRAWAL PERIOD(S)**

Not applicable.

**11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children. Store below 25 °C. Do not use after the expiry date stated on the label or blister after EXP.

**12. SPECIAL WARNING(S)**

Special warnings for each target species:

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

Special precautions for use in animals:

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.

Interaction with other medicinal products and other forms of interaction:

Onsior 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 Onsior. 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 Onsior 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 (symptoms, emergency procedures, 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.

**13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY**

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

**14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

Detailed information on this product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

**15. OTHER INFORMATION**

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

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.

For any information about this veterinary medicinal product, please contact the marketing authorisation holder.

**PACKAGE LEAFLET:**  
**Onsior 20 mg/ml solution for injection for cats and dogs**

**1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT**

Marketing authorisation holder:

Elanco GmbH  
Heinz-Lohmann-Str. 4  
27472 Cuxhaven  
Germany

Manufacturer responsible for the batch release:

Elanco France S.A.S  
26 Rue de la Chapelle  
68330 Huningue  
FRANCE

**2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

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

**3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)**

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

The solution for injection is a clear, colourless to slightly coloured (pink) liquid.

**4. INDICATION(S)**

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. ADVERSE REACTIONS**

Cats:

Gastrointestinal adverse events (vomiting, soft faeces or diarrhoea) were commonly reported, but most cases were mild and recovered without treatment. Diarrhoea or vomiting with blood were uncommon. Pain at injection site was commonly reported.

Dogs:

Adverse reactions of the digestive tract (diarrhoea and vomiting) were commonly reported but most cases were mild and recovered without treatment. Soft and dark faeces or reduced appetite were uncommon.

Slight pain at injection site was commonly reported. Moderate or severe pain at injection site was uncommon.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

## **7. TARGET SPECIES**

Cats and dogs.

## **8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION**

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 PERIOD(S)**

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 after the expiry date stated on the label after EXP. 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 WARNING(S)**

### Special precautions for use in animals:

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:

Onsior 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 Onsior. 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 Onsior 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.

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

### Overdose (symptoms, emergency procedures, antidotes):

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.

### **13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY**

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

### **14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED**

Detailed information on this product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

### **15. OTHER INFORMATION**

Onsior solution for injection for cats and dogs is available in a cardboard box containing 1 vial with 20 ml solution for injection.

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.

For any information about this veterinary medicinal product, please contact the marketing authorisation holder.