SUMMARY OF PRODUCT CHARACTERISTICS

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

i). 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.

ii). Special precautions to be take 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.

iii). Other precautions
Not applicable.

4.6 Adverse reactions (frequency and seriousness)

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 / 1000 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 / 1000 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 its local representative or the national competent authority via the national reporting system. See also the last section of the package leaflet for contact details.

4.7 Use during pregnancy, lactation or lay

Pregnancy and laction:
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 for breeding.

4.8 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.

4.9 Amount(s) 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:

ATC Vet 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_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.

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_{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.

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

Medicines should not be disposed of via wastewater.
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 Strasse 4
Groden
D-27472 Cuxhaven
Germany

8. MARKETING AUTHORISATION NUMBER

Vm 52127/5021

9. DATE OF FIRST AUTHORISATION

16 December 2008

10. DATE OF REVISION OF THE TEXT

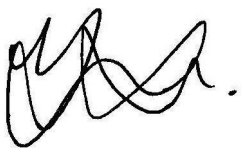
October 2023

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.



Approved: 12 October 2023