

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Galliprant 100 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Grapiprant 100 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

100 mg tablet: A brown speckled, biconvex oval tablet with the debossed number '100' on one half and the letters 'MG' on the other half; the letter 'G' is debossed on the other face.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For the treatment of pain associated with mild to moderate osteoarthritis in dogs.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or any of the excipients.

Do not use in pregnant, lactating or breeding animals. See section 4.7.

4.4 Special warnings for each target species

The majority of clinical cases assessed in the clinical field studies suffered from mild to moderate osteoarthritis based on the veterinary assessment. To achieve a substantiated response to treatment, use the veterinary medicinal product only in mild and moderate cases of osteoarthritis.

From the two clinical field studies, the overall success rates based on CBPI (Canine Brief Pain Inventory, as completed by the owner) at 28 days after the start of the treatment, were 51.3% (120/235) for Galliprant and 35.5% (82/231) for the placebo

group. This difference in favour of Galliprant was statistically significant (p-value= 0.0008).

A clinical response to treatment is usually seen within 7 days. If no clinical improvement is apparent after 14 days, treatment with Galliprant should be discontinued and different treatment options should be explored in consultation with the veterinarian.

4.5 Special precautions for use

Special precautions for use in animals

Grapiprant is a methylbenzenesulfonamide. It is not known whether dogs with a history of hypersensitivity to sulphonamides will exhibit hypersensitivity to grapiprant. If signs of sulphonamide hypersensitivity occur, treatment should be discontinued.

Mild decreases in serum albumin and total protein, most often within the reference range, have been observed in dogs treated with grapiprant but were not associated with any clinically significant observations or events.

Use with caution in dogs suffering from pre-existing liver, cardiovascular or renal dysfunctions or from gastrointestinal disease.

The concurrent use of grapiprant with other anti-inflammatory agents has not been studied and should be avoided.

The safety of the veterinary medicinal product has not been established in dogs under 9 months of age and in dogs weighing less than 3.6 kg.

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

Wash hands after handling of the veterinary medicinal product.

In case of accidental ingestion by children, mild and reversible gastrointestinal signs and nausea may be observed. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Vomiting was observed very commonly in clinical studies. Soft-formed faeces, diarrhoea and inappetence were commonly observed in clinical studies. These signs were generally transient.

Elevated liver enzymes, elevated BUN, elevated creatinine, haematemesis and haemorrhagic diarrhoea have been reported very rarely following use post authorisation.

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, lactating or breeding animals as the safety of grapiprant 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

Prior treatment with other anti-inflammatory substances may result in additional or increased severity of adverse effects and accordingly a treatment-free period with such veterinary medicinal products should be observed before the commencement of treatment with this veterinary medicinal product. The treatment-free period should take into account the pharmacokinetic properties of the products used previously.

The concomitant use of protein-bound veterinary medicinal products with grapiprant has not been studied. Commonly used protein-bound veterinary medicinal products include cardiac, anticonvulsant and behavioural medications. Drug compatibility should be monitored in animals requiring adjunctive therapy.

4.9 Amounts to be administered and administration route

For oral use.

Administer this veterinary medicinal product on an empty stomach (e.g. in the morning) and at least one hour before the next meal, once daily at a target dose of 2 mg per kg body weight.

Duration of treatment will depend on the response observed to treatment. As field studies were limited to 28 days, longer-term treatment should be considered carefully and regular monitoring undertaken by the veterinarian. Since clinical signs of canine osteoarthritis wax-and-wane, intermittent treatment may be beneficial in some dogs.

The following number of tablets should be given once daily:

Body weight (kg)	20 mg tablet	60 mg tablet	100 mg tablet	Dose range (mg/kg bw)
3.6-6.8	0.5			1.5-2.7
6.9-13.6	1			1.5-2.9
13.7-20.4		0.5		1.5-2.2
20.5-34.0		1		1.8-2.9
34.1-68.0			1	1.5-2.9
68.1-100.0			2	2.0-2.9

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

In healthy dogs treated with grapiprant for 9 consecutive months, mild and transient soft-formed or mucous faeces, occasionally bloody, and vomiting were observed at daily overdoses of approximately 2.5x and 15x the recommended dose. Grapiprant

did not produce any signs of kidney or liver toxicity at daily overdoses of up to 15x the recommended dose.

In case of overdose, symptomatic treatment should be initiated.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Other anti-inflammatory and antirheumatic agents, non-steroids

ATCvet code: QM01AX92

5.1 Pharmacodynamic properties

Grapiprant is a non-steroidal, non-cyclooxygenase inhibiting anti-inflammatory drug in the piroxicam class. Grapiprant is a selective antagonist of the EP4 receptor, a key prostaglandin E₂ receptor that predominantly mediates prostaglandin E₂-elicited nociception. The specific effects of the binding of prostaglandin E₂ to the EP4 receptor include vasodilation, increased vascular permeability, angiogenesis and production of pro-inflammatory mediators. The EP4 receptor is important in mediating pain and inflammation as it is the primary mediator of the prostaglandin E₂-elicited sensitization of sensory neurons and prostaglandin E₂-elicited inflammation.

5.2 Pharmacokinetic particulars

Absorption

Grapiprant is readily and rapidly absorbed from the gastrointestinal tract in dogs. After a single oral dose of 2 mg grapiprant/kg, C_{max} and AUC values of 1.21 µg/ml and 2.71 µg.h/ml were reached in the fasted state. Maximum grapiprant concentrations are observed in serum within one hour of dosing in the fasted state. Intake of the tablet with food reduces the oral bioavailability, i.e. the oral bioavailability of grapiprant when taken in the fasted state was 89% and when taken with food it was 33%, with mean C_{max} and AUC grapiprant values reduced 4-fold and 2-fold, respectively. Grapiprant does not accumulate in the dog after repeated administration. No gender related differences in absorption are observed.

Distribution

In vitro protein binding of grapiprant indicates that grapiprant is primarily bound to dog serum albumin. The mean percentage of unbound grapiprant was 4.35% and 5.01% at a grapiprant concentration of 200 ng/ml and 1000 ng/ml.

Biotransformation

Grapiprant is primarily bound to serum proteins. In dogs, grapiprant is a major excretion product in bile, faeces and urine. Four metabolites are identified and the metabolic pathways include N-deamination to form the major metabolite in faeces (7.2%) and urine (3.4%). Two hydroxylated metabolites and one N-oxidated

metabolite are also recovered in bile, faeces and/or urine. The pharmacological activity of the metabolites is not known.

Elimination

Grapiprant is primarily excreted via faeces. Approximately 70-80% of the administered dose is excreted within 48-72 h with the majority of the dose excreted unchanged. Faecal excretion accounted for roughly 65% of the dose whereas approximately 20% of the dose was excreted through urine. The elimination half-life of grapiprant is approximately 4.6 to 5.67 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pork liver powder
Lactose monohydrate
Sodium starch glycolate Type A
Sodium laurilsulfate
Copovidone
Cellulose, microcrystalline
Magnesium stearate
Silica, colloidal anhydrous

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 3 months.
Any remaining whole and half tablets should be discarded after 3 months following first opening.

6.4 Special precautions for storage

Do not store above 30 °C.
Any half tablets should be stored in the bottle.
In order to avoid any accidental ingestion, store tablets out of reach of animals.

6.5 Nature and composition of immediate packaging

Induction sealed, white, round high density polyethylene (HDPE) bottles (50 and 120 ml) with a threaded child-resistant cap with rayon coil.

Pack sizes of 7 and 30 tablets per bottle. One bottle per cardboard box.
Not all pack sizes may be marketed.

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

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

7. MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann Strasse 4
Grodan
27472 Cuxhaven
Germany

8. MARKETING AUTHORISATION NUMBER

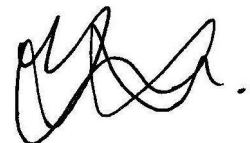
Vm 52127/5016

9. DATE OF FIRST AUTHORISATION

9 January 2018

10. DATE OF REVISION OF THE TEXT

November 2021



Approved: 12 November 2021