

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

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

Galliprant 20 mg tablets for dogs  
Galliprant 60 mg tablets for dogs  
Galliprant 100 mg tablets for dogs

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains:

### **Active substance:**

Grapiprant	20 mg
Grapiprant	60 mg
Grapiprant	100 mg

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

20 mg tablet: A brown speckled, biconvex oval tablet with a score on one face separating the debossed number '20' on one half and the letters 'MG' on the other half; the letter 'G' is debossed on the other face. The tablet can be divided into equal halves.

60 mg tablet: A brown speckled, biconvex oval tablet with a score on one face separating the debossed number '60' on one half and the letters 'MG' on the other half; the letter 'G' is debossed on the other face. The tablet can be divided into equal halves.

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 piroprant class. Grapiprant is a selective antagonist of the EP4 receptor, a key prostaglandin E<sub>2</sub> receptor that predominantly mediates prostaglandin E<sub>2</sub>-elicited nociception. The specific effects of the binding of prostaglandin E<sub>2</sub> 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 E<sub>2</sub>-elicited sensitization of sensory neurons and prostaglandin E<sub>2</sub>-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<sub>max</sub> 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<sub>max</sub> 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-Str. 4  
27472 Cuxhaven  
Germany

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

EU/2/17/221/001-006

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

Date of first authorisation: 09/01/2018

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

DD month YYYY

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

**A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer responsible for batch release

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

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

**Cardboard box (50 ml and 120 ml bottles)**

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

Galliprant 20 mg tablets for dogs  
Galliprant 60 mg tablets for dogs  
Galliprant 100 mg tablets for dogs  
grapiprant

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

20 mg grapiprant/tablet  
60 mg grapiprant/tablet  
100 mg grapiprant/tablet

**3. PHARMACEUTICAL FORM**

Tablet

**4. PACKAGE SIZE**

7 tablets  
30 tablets

**5. TARGET SPECIES**

Dogs

**6. INDICATION(S)**

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

Read the package leaflet before use.  
Oral use.

**8. WITHDRAWAL PERIOD(S)**

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

Read the package leaflet before use.

**10. EXPIRY DATE**

EXP {month/year}  
Once opened use by:....

**11. SPECIAL STORAGE CONDITIONS**

Do not store above 30 °C.  
Any half tablets should be stored in the bottle.  
Store out of reach of animals.

**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/2/17/221/001 (20 mg, 7 tablets, 50 ml bottle)  
EU/2/17/221/002 (20 mg, 30 tablets, 50 ml bottle)  
EU/2/17/221/003 (60 mg, 7 tablets, 50 ml bottle)  
EU/2/17/221/004 (60 mg, 30 tablets, 50 ml bottle)  
EU/2/17/221/005 (100 mg, 7 tablets, 50 ml bottle)  
EU/2/17/221/006 (100 mg, 30 tablets, 120 ml bottle)

**17. MANUFACTURER'S BATCH NUMBER**

Lot {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**Bottle (120 ml)**

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

Galliprant 100 mg tablets for dogs  
grapiprant

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

100 mg grapiprant

**3. PACKAGE SIZE**

30 tablets

**4. TARGET SPECIES**

Dogs

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

Read the package leaflet before use.  
Oral use.

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

Read the package leaflet before use.

**7. EXPIRY DATE**

EXP {month/year}  
Once opened use by:

**8. SPECIAL STORAGE CONDITIONS**

Do not store above 30 °C.  
Any half tablets should be stored in the bottle.  
Store out of reach of animals.

**9. 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.

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

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

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

EU/2/17/221/006 (100 mg, 30 tablets, 120 ml bottle)

**12. MANUFACTURER'S BATCH NUMBER**

Lot {number}

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

**Bottle (50 ml)**

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

Galliprant 20 mg tablets for dogs  
Galliprant 60 mg tablets for dogs  
Galliprant 100 mg tablets for dogs  
grapiprant

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

20 mg grapiprant  
60 mg grapiprant  
100 mg grapiprant

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

7 tablets  
30 tablets

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

Oral use.

**5. BATCH NUMBER**

Lot {number}

**6. EXPIRY DATE**

EXP {month/year}  
Once opened use by: ...

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

For animal treatment only.

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET:**  
**Galliprant 20 mg tablets for dogs**  
**Galliprant 60 mg tablets for dogs**  
**Galliprant 100 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 batch release:

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

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

Galliprant 20 mg tablets for dogs  
Galliprant 60 mg tablets for dogs  
Galliprant 100 mg tablets for dogs  
grapiprant

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

One tablet contains:

**Active substance:**

Grapiprant	20 mg
Grapiprant	60 mg
Grapiprant	100 mg

20 mg tablet: A brown speckled, biconvex oval tablet with a score on one face separating the debossed number '20' on one half and the letters 'MG' on the other half; the letter 'G' is debossed on the other face. The tablet can be divided into equal halves.

60 mg tablet: A brown speckled, biconvex oval tablet with a score on one face separating the debossed number '60' on one half and the letters 'MG' on the other half; the letter 'G' is debossed on the other face. The tablet can be divided into equal halves.

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. INDICATION(S)**

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

## **5. 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.

## **6. ADVERSE REACTIONS**

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)

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**

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

## **9. ADVICE ON CORRECT ADMINISTRATION**

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 drugs 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.

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

Not applicable.

## **11. SPECIAL STORAGE PRECAUTIONS**

Keep out of the sight and reach of children.

In order to avoid any accidental ingestion, store tablets out of reach of animals.

Do not store above 30 °C.

Any half tablets should be stored in the bottle.

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

Shelf-life after first opening of the bottle: 3 months. Any remaining whole and half tablets should be discarded after 3 months following first opening of the bottle.

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

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.

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.

Interaction with other medicinal products and other forms of interaction:

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.

Pregnancy:

Do not use in pregnant animals as the safety of grapiprant has not been established during pregnancy.

Lactation:

Do not use lactating animals as the safety of grapiprant has not been established during lactation.

Fertility:

Do not use in breeding animals as the safety of grapiprant has not been established or in dogs used for breeding.

Overdose (symptoms, emergency procedures, antidotes):

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.

**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 veterinary medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu/>.

**15. OTHER INFORMATION**

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 E<sub>2</sub> receptor that predominantly mediates prostaglandin E<sub>2</sub>-elicited nociception. The specific effects of the binding of prostaglandin E<sub>2</sub> 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 E<sub>2</sub>-elicited sensitization of sensory neurons and prostaglandin E<sub>2</sub>-elicited inflammation.

Grapiprant is readily and rapidly absorbed from the gastrointestinal tract in dogs. Grapiprant is mainly excreted via faeces.

The veterinary medicinal product is available in the following pack sizes:  
One white HDPE bottle with a child-resistant cap containing 7 or 30 tablets (20 mg, 60 mg or 100 mg tablets). Not all pack sizes may be marketed.