ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prevomax 10 mg/ml solution for injection for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substance:

Maropitant 10 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	11.1 mg
Betadex sulfobutyl ether sodium	
Citric acid, anhydrous	
Sodium hydroxide	
Water for injections	

A clear, colourless to light yellow solution

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats.

3.2 Indications for use for each target species

Dogs

- For the treatment and prevention of nausea induced by chemotherapy.
- For the prevention of vomiting except that induced by motion sickness.
- For the treatment of vomiting, in combination with other supportive measures.
- For the prevention of perioperative nausea and vomiting and improvement in recovery from general anaesthesia after use of the μ-opiate receptor agonist morphine.

Cats

- For the prevention of vomiting and the reduction of nausea, except that induced by motion sickness.
- For the treatment of vomiting, in combination with other supportive measures.

3.3 Contraindications

None.

3.4 Special warnings

Vomiting can be associated with serious, severely debilitating conditions including gastrointestinal obstructions; therefore, appropriate diagnostic evaluations should be employed.

Good veterinary practice indicates that antiemetics should be used in conjunction with other veterinary and supportive measures such as dietary control and fluid replacement therapy while addressing the underlying causes of the vomiting.

The use of the veterinary medicinal product against vomiting due to motion sickness is not recommended.

Dogs:
Although maropitant has been demonstrated to be effective in both the treatment and prevention of emesis induced by chemotherapy, it was found more efficacious if used preventively. Therefore, it is recommended to administer the veterinary medicinal product prior to administration of the chemotherapeutic agent.

Cats:
The efficacy of maropitant in reduction of nausea was demonstrated in studies using a model (xylazine-induced nausea).

3.5 Special precautions for use

Special precautions for safe use in the target species:

The safety of maropitant has not been established in dogs less than 8 weeks of age, or in cats less than 16 weeks of age, and in pregnant or lactating dogs and cats. Use only according to the benefit-risk assessment by the responsible veterinarian.

Maropitant is metabolised in the liver and therefore should be used with caution in patients with hepatic disease. As maropitant is accumulated in the body during a 14 day treatment period due to metabolic saturation, careful monitoring of liver function and any adverse events should be implemented during long term treatment.

The veterinary medicinal product should be used with caution in animals suffering from or with predisposition for cardiac diseases as maropitant has affinity to Ca- and K-ion channels. Increases of approximately 10% in the QT interval of the ECG were observed in a study on healthy Beagle dogs administered 8 mg/kg orally; however, such an increase is unlikely to be of clinical significance.

Due to the frequent occurrence of transient pain during subcutaneous injection, appropriate animal restraining measures may have to be applied. Injecting the product at refrigerated temperature may reduce pain at injection.

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

People with known hypersensitivity to maropitant should administer the veterinary medicinal product with caution.

Wash hands after use. In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician. In laboratory studies, maropitant has been shown to be a potential eye irritant. In the case of accidental eye exposure, flush the eyes with plenty of water and seek medical attention.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Target species: Dog, cat

Very common (>1 animal / 10 animals treated):	Injection site pain[a]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic-type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) Lethargy Ataxia, Convulsion, Seizure, Muscle tremor
Undetermined frequency	Injection site pain[b]

[a] in cats - moderate to severe (in approximately one third of cats) when injected subcutaneously.
[b] in dogs - when injected subcutaneously.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See section `Contact details´ of the package leaflet.

3.7 Use during pregnancy, lactation or lay

Use only according to the benefit-risk assessment by the responsible veterinarian, because conclusive reproductive toxicity studies have not been conducted in any animal species.

3.8 Interaction with other medicinal products and other forms of interaction

The veterinary medicinal product should not be used concomitantly with Ca-channel antagonists as maropitant has affinity to Ca-channels.
Maropitant is highly bound to plasma proteins and may compete with other highly bound medicines.

3.9 Administration routes and dosage

For subcutaneous or intravenous use in dogs and cats.

The veterinary medicinal product solution for injection should be injected subcutaneously or intravenously, once daily, at a dose of 1 mg of maropitant / kg bodyweight (1 ml/10 kg bodyweight) for up to 5 consecutive days. Intravenous administration of the veterinary medicinal product should be given as a single bolus without mixing the product with any other fluids.

To prevent vomiting, the veterinary medicinal product solution for injection should be administered more than 1 hour in advance. The duration of effect is approximately 24 h and therefore treatment can be given the night before administration of an agent that may cause emesis e.g. chemotherapy.

As the pharmacokinetic variation is large and maropitant accumulates in the body after once daily repeated administration, lower doses than recommended might be sufficient in some individuals and when repeating the dose.

For administration by subcutaneous injection, see also “special precautions for safe use in target species” (section 3.5).

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Apart from transient reactions at the injection site following subcutaneous administration, maropitant was well tolerated in dogs and young cats injected daily with up to 5 mg/kg bodyweight (5 times the recommended dose) for 15 consecutive days (3-times the recommended duration of administration). No data have been presented on overdoses in adult cats.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QA04AD90

4.2 Pharmacodynamics

Vomiting is a complex process coordinated centrally by the emetic centre. This centre consists of several brainstem nuclei (area postrema, nucleus tractus solitarius, dorsal motor nucleus of the vagus nerve) that receive and integrate sensory stimuli from central and peripheral sources and chemical stimuli from the circulation and the cerebro-spinal fluid. Maropitant is a neurokinin 1 (NK_1) receptor antagonist, which acts by inhibiting the binding of substance P, a neuropeptide of the tachykinin family. Substance P is found in significant concentrations in the nuclei comprising the emetic centre and is considered the key neurotransmitter involved in vomiting. By inhibiting the binding of substance P within the emetic centre, maropitant is effective against neural and humoral (central and peripheral) causes of vomiting.

A variety of *in vitro* assays have demonstrated that maropitant binds selectively at the NK_1 receptor with dose-dependent functional antagonism of substance P activity.

Maropitant is effective against vomiting. The anti-emetic efficacy of maropitant against central and peripheral emetics was demonstrated in experimental studies including apomorphine, cisplatin and syrup of ipecac (dogs) and xylazine (cats).
Signs of nausea in dogs including excessive salivation and lethargy might remain after treatment.

4.3 Pharmacokinetics

Dogs:
The pharmacokinetic profile of maropitant when administered as a single subcutaneous dose of 1 mg/kg bodyweight to dogs was characterised by a maximum concentration (C_{max}) in plasma of approximately 92 ng/ml; this was achieved within 0.75 hours post-dosing (T_{max}). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{1/2}$) of 8.84 hours. Following a single intravenous dose at 1 mg/kg the initial plasma concentration was 363 ng/ml. The volume of distribution at steady-state (V_{ss}) was 9.3 l/kg and systemic clearance was 1.5 l/h/kg. The elimination $t_{1/2}$ following intravenous dosing was approximately 5.8 h.

During clinical studies maropitant plasma levels conferred efficacy from 1 hour after administration.

The bioavailability of maropitant after subcutaneous administration in dogs was 90.7%. Maropitant displays linear kinetics when administered subcutaneously within the 0.5–2 mg/kg dose range.

Following repeated subcutaneous administration of once-daily doses of 1 mg/kg bodyweight for five consecutive days, accumulation was 146%. Maropitant undergoes cytochrome P450 (CYP) metabolism in the liver. CYP2D15 and CYP3A12 were identified as the canine isoforms involved in the hepatic biotransformation of maropitant.

Renal clearance is a minor route of elimination, with less than 1% of a 1 mg/kg subcutaneous dose appearing in the urine as either maropitant or its major metabolite. Plasma protein binding of maropitant in dogs is more than 99%.

Cats:
The pharmacokinetic profile of maropitant when administered as a single subcutaneous dose of 1 mg/kg body weight to cats was characterised by a maximum concentration (C_{max}) in plasma of approximately 165 ng/ml; this was achieved on average 0.32 hours (19 min) post-dosing (T_{max}). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{1/2}$) of 16.8 hours. Following a single intravenous dose at 1 mg/kg the initial plasma concentration was 1040 ng/ml. The volume of distribution at steady-state (V_{ss}) was 2.3 l/kg and systemic clearance was 0.51 l/h/kg. The elimination $t_{1/2}$ following intravenous dosing was approximately 4.9 h. There appears to be an age-related effect on the pharmacokinetics of maropitant in cats with kittens having higher clearance than adults.

During clinical studies maropitant plasma levels conferred efficacy from 1 hour after administration.

The bioavailability of maropitant after subcutaneous administration in cats was 91.3%. Maropitant displays linear kinetics when administered subcutaneously within the 0.25–3 mg/kg dose range.

Following repeated subcutaneous administration of once-daily doses of 1 mg/kg bodyweight for five consecutive days, accumulation was 250%. Maropitant undergoes cytochrome P450 (CYP) metabolism in the liver. CYP1A and CYP3A-related enzymes were identified as the feline isoforms involved in the hepatic biotransformation of maropitant.

Renal and faecal clearances are minor routes of elimination for maropitant, with less than 1% of a 1 mg/kg subcutaneous dose appearing in the urine or faeces as maropitant. For the major metabolite 10.4% of the maropitant dose was recovered in urine and 9.3% in faeces. Plasma protein binding of maropitant in cats was estimated to be 99.1%.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 56 days.

5.3 Special precautions for storage

Do not freeze.

5.4 Nature and composition of immediate packaging

Amber glass type I vial closed with a coated bromobutyl rubber stopper and aluminium cap in a cardboard box.
Pack sizes of 1 vial of 10 ml, 20 ml, 25 ml or 50 ml.

Not all pack sizes may be marketed.

5.5 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 or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/17/211/001-004

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 19/06/2017

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

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
Outer carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prevomax 10 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

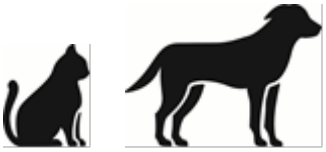
10 mg/ml maropitant

3. PACKAGE SIZE

10 ml
20 ml
25 ml
50 ml

4. TARGET SPECIES

Dogs, cats



5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous or intravenous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 56 days.

9. SPECIAL STORAGE PRECAUTIONS

Do not freeze.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/17/211/00110 ml
EU/2/17/211/002 20 ml
EU/2/17/211/003 25 ml
EU/2/17/211/004 50 ml

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Glass vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prevomax

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

10 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 56 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Prevomax 10 mg/ml solution for injection for dogs and cats

2. Composition

1 ml contains:

Active substance:
Maropitant 10 mg

Excipients:
Benzyl alcohol (E1519) 11.1 mg

A clear, colourless to light yellow solution.

3. Target species

Dogs and cats.


4. Indications for use

Dogs
- For the treatment and prevention of nausea induced by chemotherapy.
- For the prevention of vomiting except that induced by motion sickness.
- For the treatment of vomiting, in combination with other supportive measures.
- For the prevention of perioperative nausea and vomiting and improvement in recovery from general anaesthesia after use of the μ-opiate receptor agonist morphine.

Cats
- For the prevention of vomiting and the reduction of nausea, except that induced by motion sickness.
- For the treatment of vomiting, in combination with other supportive measures.

5. Contraindications

None.

6. Special warnings

Special warnings:
Vomiting can be associated with serious, severely debilitating conditions and the cause should be investigated. Products such as Prevomax should be used in conjunction with other supportive

measures such as dietary control and fluid replacement therapy, as recommended by your veterinary surgeon.

Maropitant is metabolised in the liver and therefore should be used with caution in dogs and cats with liver disease. Prevomax should be used with caution in animals suffering from or with predisposition for heart diseases.

The use of Prevomax solution for injection against vomiting due to motion sickness is not recommended.

Dogs:
Although maropitant has been demonstrated to be effective in both the treatment and prevention of emesis induced by chemotherapy, it was found more efficacious if used preventively. Therefore, it is recommended to administer the veterinary medicinal product prior to administration of the chemotherapeutic agent.

Cats:
The efficacy of maropitant in reduction of nausea in cats was demonstrated in studies using a model (xylazine-induced nausea).

Special precautions for safe use in the target species:
The safety of maropitant has not been established in dogs less than 8 weeks of age, or in cats less than 16 weeks of age, or in pregnant or lactating dogs and cats. The responsible veterinarian should make a benefit-risk assessment before using the veterinary medicinal product in dogs less than 8 weeks of age, or in cats less than 16 weeks of age, or in pregnant or lactating bitches and cats.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to maropitant should administer the veterinary medicinal product with caution.
Wash hands after use. In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician. Maropitant has been shown to be a potential eye irritant, and in the case of accidental eye exposure, flush the eyes with plenty of water and seek medical attention.

Pregnancy and lactation:
Use only according to the benefit-risk assessment by the responsible veterinarian, because conclusive reproductive toxicity studies have not been conducted in any animal species.

Interaction with other medicinal products and other forms of interaction:
The veterinary medicinal product should not be used concomitantly with Ca-channel antagonists as maropitant has affinity to Ca-channels.
Maropitant is highly bound to plasma proteins and may compete with other highly bound medicines.

Overdose:
Apart from transient reactions at the injection site following subcutaneous administration, maropitant was well tolerated in dogs and young cats injected daily with up to 5 mg/kg bodyweight (5 times the recommended dose) for 15 consecutive days (3-times the recommended duration of administration). No data have been presented on overdoses in adult cats.

Major incompatibilities:
Prevomax must not be mixed with other veterinary medicinal products in the same syringe as its compatibility with other products has not been tested

7. Adverse events

Target species: Dog, cat

Very common (>1 animal / 10 animals treated):	Injection site pain[a]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic-type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) Lethargy Ataxia, Convulsion, Seizure, Muscle tremor
Undetermined frequency	Injection site pain[b]

[a] in cats - moderate to severe (in approximately one third of cats) when injected subcutaneously.
[b] in dogs - when injected subcutaneously.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

For subcutaneous or intravenous use in dogs and cats.

Prevomax solution for injection should be injected subcutaneously or intravenously, once daily, at a dose of 1 mg of maropitant/kg bodyweight (1 ml/10 kg bodyweight). Treatment may be repeated for up to five consecutive days. Intravenous administration of Prevomax should be given as a single bolus without mixing the product with any other fluids.

9. Advice on correct administration

To prevent vomiting, Prevomax solution for injection should be administered more than 1 hour in advance. The duration of effect is approximately 24 h and therefore treatment can be given the night before administration of an agent that may cause emesis, e.g. chemotherapy.

Due to the frequent occurrence of transient pain during subcutaneous injection, appropriate animal restraining measures may have to be applied. Injecting the product at refrigerated temperature may reduce pain at injection.

As the pharmacokinetic variation is large and maropitant accumulates in the body after once daily repeated administration, lower doses than recommended might be sufficient in some individuals and when repeating the dose.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and the vial label after Exp. The expiry date refers to the last day of that month.
Shelf life after first opening the vial: 56 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Marketing authorisation numbers:
EU/2/17/211/001-004

Amber glass type I vial closed with a coated bromobutyl rubber stopper and aluminium cap in a cardboard box.
Pack sizes of 1 vial of 10 ml, 20 ml, 25 ml or 50 ml.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands
Tel.: +31 348 563434

Manufacturer responsible for batch release:

Produlab Pharma B.V.
Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands