

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:

Benzyl alcohol (E1519) 11.1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

A clear, colourless to light yellow solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats.

4.2 Indications for use, specifying the 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.

4.3 Contraindications

None.

4.4 Special warnings for each target species

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).

4.5 Special precautions for use

Special precautions for use in animals

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.

4.6 Adverse reactions (frequency and seriousness)

Pain at injection site may occur when injected subcutaneously. In cats, moderate to severe response to injection is very commonly observed (in approximately one third of cats).

In very rare cases, anaphylactic type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) may occur.

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

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.

4.8 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.

4.9 Amounts to be administered and administration route

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 use in animals” (section 4.5).

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

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 (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.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiemetics.

ATCvet code: QA04AD90

5.1 Pharmacodynamic properties

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) 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 (NK₁) 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 NK₁ 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.

5.2 Pharmacokinetic particulars

Dogs:

The pharmacokinetic profile of maropitant when administered as a single subcutaneous dose of 1 mg/kg body weight 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%.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Betadex sulfobutyl ether sodium
Benzyl alcohol (E1519)
Citric acid, anhydrous
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 in the same syringe.

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: 56 days.

6.4. Special precautions for storage

Do not freeze.

6.5 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.

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/17/211/001-004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19/06/2017

10. DATE OF REVISION OF THE TEXT

<{MM/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**
- D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the 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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable.

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Specific pharmacovigilance requirements:

The PSURs for Prevomax shall be submitted at the same frequency as for Cerenia (reference product).

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 for dogs and cats
maropitant



2. STATEMENT OF ACTIVE SUBSTANCES

10 mg/ml maropitant

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml
20 ml
25 ml
50 ml

5. TARGET SPECIES

Dogs, cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

SC, IV
Read the package leaflet before use.

Comment:

Given the small vial size(s), would it not be preferable to replace these by "SC, IV"

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

Once broached use within 56 days.

11. SPECIAL STORAGE CONDITIONS

Do not freeze.

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

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/17/211/001-004

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Glass vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prevomax 10 mg/ml injection
maropitant



2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

10 mg/ml

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

10 ml
20 ml
25 ml
50 ml

4. ROUTE(S) OF ADMINISTRATION

SC, IV

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

Lot:

7. EXPIRY DATE

EXP
Once broached use within 56 days.

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Prevomax 10 mg/ml solution for injection for dogs and 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:

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

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

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

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

1 ml contains:

Active substance:

Maropitant 10 mg

Excipients:

Benzyl alcohol (E1519) 11.1 mg

A clear, colourless to light yellow solution.

4. INDICATION(S)

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. ADVERSE REACTIONS

Pain at injection site may occur when injected subcutaneously.

In cats, moderate to severe response to injection is very commonly observed (in approximately one third of cats).

In very rare cases, anaphylactic type reactions (allergic oedema, urticaria, erythema, collapse, dyspnoea, pale mucous membranes) may occur.

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 and cats.



8. DOSAGE FOR EACH SPECIES, ROUTE(S) 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 body weight (1 ml/10 kg body weight). 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 PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not freeze.

Shelf life after first opening the vial: 56 days.

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

12. SPECIAL WARNING(S)

Special warnings for each target species:

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 use in animals:

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 drugs.

Overdose (symptoms, emergency procedures, 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 (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.

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.

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

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

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

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.