

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cerenia 16 mg tablets for dogs
Cerenia 24 mg tablets for dogs
Cerenia 60 mg tablets for dogs
Cerenia 160 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each tablet contains 16 mg, 24 mg, 60 mg or 160 mg maropitant as maropitant citrate monohydrate.

Excipients:

Each tablet contains 0.075% w/w Sunset Yellow (E110) as a colorant.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Pale orange tablet.

The tablets have a score line allowing the tablet to be halved, with the letters “MPT” and figures denoting the quantity of maropitant on one side, the reverse side is blank.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

- For the prevention of nausea induced by chemotherapy.
- For the prevention of vomiting induced by motion sickness.
- For the prevention and treatment of vomiting, in conjunction with Cerenia solution for injection and 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.

Cerenia tablets have been shown to be effective in the treatment of emesis, however where the frequency of vomiting is high, orally administered Cerenia may not be absorbed before the next vomiting event occurs. It is therefore recommended to initiate the treatment of emesis with Cerenia solution for injection.

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 safety of maropitant during treatment beyond 5 days has not been explored in the target population (i.e. young dogs suffering from viral enteritis). In case treatment

for a longer period than 5 days is regarded as necessary, careful monitoring of potential adverse events should be implemented.

4.5 Special precautions for use

Special precautions for use in animals

The safety of the veterinary medicinal product has not been established in dogs less than 16 weeks of age for the 8 mg/kg dose (motion sickness), and in dogs less than 8 weeks of age for the 2 mg/kg dose (vomiting) as well as in pregnant or lactating bitches. 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 in addition to any adverse events should be implemented during long term treatment.

Cerenia 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.

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 ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Incidents of pre-travel vomiting, usually within two hours post-dosing were commonly reported after administration of the 8 mg/kg dose.

Lethargy has been reported in very rare cases, based on post-marketing safety experience.

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

Cerenia 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.

4.9 Amounts to be administered and administration route

For oral use.

For motion sickness, a light meal or snack before dosing is recommended; prolonged fasting before administration should be avoided. However, Cerenia tablets should not be administered wrapped or encapsulated in food as this may delay dissolution of the tablet and consequently the onset of efficacy.

Dogs should be carefully observed following administration to ensure that each tablet is swallowed.

For the prevention of nausea induced by chemotherapy and treatment and prevention of vomiting (except motion sickness), (only for dogs 8 weeks of age or older).

To treat or prevent vomiting, Cerenia tablets should be administered once daily, at a dose of 2 mg maropitant per kg bodyweight, using the number of tablets given in the table below. Tablets are breakable along the score line on the tablet.

To prevent vomiting, tablets should be given more than 1 hour in advance. The duration of the effect is approximately 24 hours and, therefore, tablets can be given the night before administration of an agent that may cause emesis (e.g. chemotherapy).

Cerenia can be used to treat or prevent vomiting either as tablets or as solution for injection administered once daily. Cerenia solution for injection may be administered for up to five days and Cerenia tablets for up to fourteen days.

Prevention of nausea induced by chemotherapy Treatment and prevention of vomiting (except motion sickness)			
Dog body weight (kg)	Number of tablets		
	16 mg	24 mg	60 mg
3.0–4.0*	½		
4.1–8.0	1		
8.1–12.0		1	
12.1–24.0		2	
24.1–30.0			1
30.1–60.0			2

* Correct dose for dogs of less than 3 kg cannot be accurately achieved.

For prevention of vomiting induced by motion sickness, (only for dogs 16 weeks of age or older)

To prevent vomiting induced by motion sickness, Cerenia tablets should be administered once daily, at a dose of 8 mg maropitant per kg bodyweight, using the numbers of tablets given in the table below. Tablets are breakable along the score line on the tablet.

Tablets should be administered at least one hour before starting the journey. The anti-emetic effect persists for at least 12 hours, which for convenience may allow administration the night before early morning travel. Treatment may be repeated for a maximum of two consecutive days.

Prevention of motion sickness				
Dog body weight (kg)	Number of tablets			
	16 mg	24 mg	60 mg	160 mg
1.0–1.5		½		
1.6–2.0	1			
2.1–3.0		1		
3.1–4.0	2			
4.1–6.0		2		
6.1–7.5			1	
7.6–10.0				½
10.1–15.0			2	
15.1–20.0				1
20.1–30.0				1½
30.1–40.0				2
40.1–60.0				3

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.

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

Cerenia tablets were well tolerated when administered for 15 days at dosages up to 10 mg/kg bodyweight per day.

Clinical signs including vomiting on first administration, excess salivation and watery faeces have been observed when the product has been administered at doses in excess of 20 mg/kg.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiemetics.

ATCvet code: QA04AD90.

Maropitant is a potent and selective neurokinin (NK-1) receptor antagonist, which acts by inhibiting the binding of substance P, a neuropeptide of the tachykinin family, in the CNS.

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. *In vivo* studies in dogs demonstrated the anti-emetic

efficacy of maropitant against central and peripheral emetics including apomorphine, cisplatin and syrup of ipecac.

Maropitant is non-sedative and should not be used as a sedative in motion sickness.

Maropitant is effective against vomiting. Signs of nausea including excessive salivation and lethargy might remain during treatment.

5.2 Pharmacokinetic particulars

The pharmacokinetic profile of maropitant when administered as a single oral dose of 2 mg/kg body weight to dogs was characterised by a maximum concentration ($C_{\max}$) in plasma of approximately 81 ng/ml; this was achieved within 1.9 hours post-dosing ($T_{\max}$). Peak concentrations were followed by a decline in systemic exposure with an apparent elimination half-life ($t_{0.5}$) of 4.03 hours. At a dose of 8 mg/kg, $C_{\max}$ of 776 ng/ml was reached at 1.7 hours post-dosing. The elimination half-life at 8 mg/kg was 5.47 hours.

The inter-individual variation in kinetics may be large, up to 70 CV% for AUC.

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

Estimates for the oral bioavailability of maropitant were 23.7% at 2 mg/kg and 37.0% at 8 mg/kg. The volume of distribution at steady-state (V_{ss}) determined after intravenous administration at 1–2 mg/kg ranged from approximately 4.4 to 7.0 l/kg. Maropitant displays non-linear pharmacokinetics (AUC increases more than proportionally with increasing dose) when administered orally within the 1–16 mg/kg dose range.

Following repeated oral administration for five consecutive days at a daily dose of 2 mg/kg, accumulation was 151%. Following repeated oral administration for two consecutive days at a daily dose of 8 mg/kg, accumulation was 218%. 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 an 8 mg/kg oral dose appearing in the urine as either maropitant or its major metabolite. Plasma protein binding of maropitant in dogs is more than 99%.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose
Sunset Yellow (E110) as a colorant

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 of half tablets: 2 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
An unused half tablet should be returned to the opened blister and kept within the outer cardboard.

6.5 Nature and composition of immediate packaging

Cardboard box containing one aluminium-aluminium blister pack, each containing four tablets per pack.

Cerenia tablets are available in 16 mg, 24 mg, 60 mg and 160 mg strength.

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

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/06/062/001-004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29/09/2006.
Date of last renewal: 05/08/2011.

10. DATE OF REVISION OF THE TEXT

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.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of solution contains:

Active substance:

Maropitant (as maropitant citrate monohydrate) 10 mg

Excipients:

Metacresol (as preservative) 3.3 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 Cerenia solution for injection against vomiting due to motion sickness is not recommended.

Dogs:

Although Cerenia 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 antiemetic prior to administration of the chemotherapeutic agent.

Cats:

The efficacy of Cerenia 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 the veterinary medicinal product 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.

Cerenia 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).

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

Lethargy has been reported in very rare cases, based on post-marketing safety experience.

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

Cerenia 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.

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

In dogs, Cerenia can be used to treat or prevent vomiting either as tablets or as solution for injection administered once daily. Cerenia solution for injection may be administered for up to five days and Cerenia tablets for up to fourteen days.

To prevent vomiting, Cerenia solution for injection should be administered more than 1 hour in advance. The effect duration 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.

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

Apart from transient reactions at the injection site following subcutaneous administration, Cerenia solution for injection 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.

Maropitant is a potent and selective neurokinin (NK-1) receptor antagonist, which acts by inhibiting the binding of substance P, a neuropeptide of the tachykinin family, in the CNS.

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

Sulphobutyl ether β -cyclodextrin (SBECD)
Metacresol
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: 60 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Amber molded glass type 1 vial, 20 ml, chlorobutyl rubber stopper and aluminium overseal with flip-off button.
Each cardboard box contains 1 vial.

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

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/06/062/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29/09/2006.

Date of last renewal: 05/08/2011.

10. DATE OF REVISION OF THE TEXT

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. MANUFACTURERS 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. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Cerenia Tablets:

FAREVA AMBOISE
Zone Industrielle,
29 route des Industries
37530 Pocé-sur-Cisse
FRANCE

Cerenia Solution for Injection:

FAREVA AMBOISE
Zone Industrielle,
29 route des Industries
37530 Pocé-sur-Cisse
FRANCE

or

Zoetis Manufacturing & Research Spain, S.L.
Ctra. de Camprodón, s/nº
Finca La Riba
Vall de Bianya
Gerona 17813
SPAIN

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

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

With the extended use of Cerenia tablets in dogs from 5 to 14 consecutive days, the periodic safety update report (PSUR) cycle for Cerenia has been reset and the data lock point for the next PSUR is 30 June 2014 for submission of 6 monthly reports (covering all authorised presentations of the product) for the next two years, followed by yearly reports for the subsequent two years and thereafter at 3 yearly intervals.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box / Tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cerenia 16 mg tablets for dogs
Cerenia 24 mg tablets for dogs
Cerenia 60 mg tablets for dogs
Cerenia 160 mg tablets for dogs

maropitant

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains 16 mg maropitant as maropitant citrate monohydrate.
Each tablet contains 24 mg maropitant as maropitant citrate monohydrate.
Each tablet contains 60 mg maropitant as maropitant citrate monohydrate.
Each tablet contains 160 mg maropitant as maropitant citrate monohydrate.

The tablets also contain Sunset Yellow (E110) as a colorant.

3. PHARMACEUTICAL FORM

Tablets

4. PACKAGE SIZE

4 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

It is recommended to initiate treatment of emesis with Cerenia solution for injection.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS**12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY**

Disposal: read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

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

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/06/062/001 (16 mg tablets)
EU/2/06/062/002 (24 mg tablets)
EU/2/06/062/003 (60 mg tablets)
EU/2/06/062/004 (160 mg tablets)

17. MANUFACTURER’S BATCH NUMBER

Lot

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
--

BLISTER / Tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT
--

Cerenia 16 mg tablets for dogs
Cerenia 24 mg tablets for dogs
Cerenia 60 mg tablets for dogs
Cerenia 160 mg tablets for dogs
maropitant

2. NAME OF MARKETING AUTHORISATION HOLDER
--

Zoetis
(Logo)

3. EXPIRY DATE

EXP {month/year}

4. BATCH NUMBER

Lot

5. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box / Solution for injection

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cerenia 10 mg/ml solution for injection for dogs and cats
maropitant

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml of solution contains 10 mg maropitant (as maropitant citrate monohydrate).

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

20 ml

5. TARGET SPECIES

Dogs and cats

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

SC, IV
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)**9. SPECIAL WARNING(S), IF NECESSARY**

In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached, use by:.....

11. SPECIAL STORAGE CONDITIONS

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

Disposal: read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE
--

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”
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Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

16. MARKETING AUTHORISATION NUMBER(S)
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EU/2/06/062/005

17. MANUFACTURER’S BATCH NUMBER
--

Lot

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**Glass vial / Solution for injection****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Cerenia 10 mg/ml injection for dogs and cats
maropitant

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

10 mg/ml

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

20 ml

4. ROUTE(S) OF ADMINISTRATION

SC, IV

5. WITHDRAWAL PERIOD(S)**6. BATCH NUMBER**

Lot

7. EXPIRY DATE

EXP {month/year}
Once broached, use within 60 days.

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

**PACKAGE LEAFLET:
Cerenia 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:

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

Manufacturer responsible for batch release:

FAREVA AMBOISE
Zone Industrielle,
29 route des Industries
37530 Pocé-sur-Cisse
FRANCE

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cerenia 16 mg tablets for dogs
Cerenia 24 mg tablets for dogs
Cerenia 60 mg tablets for dogs
Cerenia 160 mg tablets for dogs

maropitant

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

Each tablet contains 16 mg, 24 mg, 60 mg or 160 mg maropitant as maropitant citrate monohydrate. The tablets also contain Sunset Yellow (E110) as a colourant. The tablets are pale orange and have a score line allowing the tablet to be halved, with the letters “MPT” and figures denoting the quantity of maropitant on one side, the reverse side is blank.

4. INDICATION(S)

- For the prevention of nausea induced by chemotherapy.
- For the prevention of vomiting induced by motion sickness.
- For the prevention and treatment of vomiting, in conjunction with *Cerenia solution for injection* and in combination with other supportive measures.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

Administering Cerenia on a completely empty stomach may cause your dog to vomit. Giving your dog a light meal or snack before administering the tablet could help preventing this effect. Prolonged fasting before administration should be avoided.

Cerenia is not a sedative and some motion sick dogs may show nausea-like signs during travel such as salivation and lethargy. These signs are temporary and should resolve when the journey ends.

Lethargy has been reported in very rare cases, based on post-marketing safety experience.

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.

For prevention of nausea induced by chemotherapy and treatment and prevention of vomiting (except motion sickness), only for dogs 8 weeks of age or older

To treat and/or prevent vomiting except motion sickness, Cerenia tablets should be administered once daily, at a dose of 2 mg maropitant per kg bodyweight, using the number of tablets given in the table below. Tablets are breakable along the score line on the tablet.

To prevent vomiting, tablets should be given more than 1 hour in advance. The duration of the effect is approximately 24 hours and, therefore, tablets can be given the night before administration of an agent that may cause emesis (e.g. chemotherapy).

Cerenia can be used to treat or prevent vomiting either as tablets or as solution for injection administered once daily. Cerenia solution for injection may be administered for up to five days and Cerenia tablets for up to fourteen days.

Prevention of nausea induced by chemotherapy Treatment and prevention of vomiting (except motion sickness)			
Dog body weight (kg)	Number of tablets		
	16 mg	24 mg	60 mg
3.0–4.0*	½		
4.1–8.0	1		
8.1–12.0		1	
12.1–24.0		2	
24.1–30.0			1
30.1–60.0			2

* Correct dose for dogs of less than 3 kg cannot be accurately achieved.

For prevention of vomiting induced by motion sickness, only for dogs 16 weeks of age or older

To prevent vomiting induced by motion sickness, Cerenia tablets should be administered once daily, at a dose of 8 mg maropitant per kg bodyweight, using the numbers of tablets given in the table below. Tablets are breakable along the score line on the tablet.

Tablets should be administered at least one hour before starting the journey. The anti-emetic effect persists for at least 12 hours, which for convenience may allow administration the night before early morning travel. Treatment may be repeated for a maximum of two consecutive days.

In some individual dogs and when repeating the treatment, lower doses than recommended might be sufficient.

Prevention of motion sickness only				
Dog body weight (kg)	Number of tablets			
	16 mg	24 mg	60 mg	160 mg
1.0–1.5		½		
1.6–2.0	1			
2.1–3.0		1		
3.1–4.0	2			
4.1–6.0		2		
6.1–7.5			1	
7.6–10.0				½
10.1–15.0			2	
15.1–20.0				1
20.1–30.0				1½
30.1–40.0				2
40.1–60.0				3

9. ADVICE ON CORRECT ADMINISTRATION

To remove a tablet from the blister the following sequence should be carried out;

- Firstly, fold or cut along the perforation between each tablet as shown by the scissor symbol ✂
- Find the pull-back notch (or cut) as shown by the arrow symbol ➔.
- Holding one side of the cut firmly, pull the other side towards the centre of the blister until the tablet is visible.
- Remove tablet from blister and administer as instructed.

Note: No attempt should be made to remove the tablet by pushing it through the blister backing as this will damage both the tablet and blister.

For motion sickness a light meal or snack before dosing is recommended, prolonged fasting before administration should be avoided. Cerenia tablets should not be administered wrapped or encapsulated in food as this may delay dissolution of the tablet and consequently the onset of the effect.

Dogs should be carefully observed following administration to ensure that each tablet is swallowed.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE CONDITIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

Half-tablets should be stored for a maximum of two days after removal from the blister. Half-tablets should be returned to the opened blister and kept within the cardboard outer.

Do not use this veterinary medicinal product after the expiry date which is stated on the blister after EXP.

12. SPECIAL WARNINGS

Special warnings for each target species:

Vomiting can be associated with serious, severely debilitating conditions and the cause should be investigated. Products such as Cerenia should be used in conjunction with other supportive measures such as dietary control and fluid replacement therapy, as recommended by your veterinary surgeon. The safety of maropitant during treatment beyond 5 days has not been explored in the target population (i.e. young dogs suffering from viral enteritis). In case treatment for a longer period than 5 days is regarded as necessary, careful monitoring of potential adverse events should be implemented.

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

Special precautions for use in animals:

The safety of Cerenia has not been established in dogs less than 16 weeks of age for the 8 mg/kg dose (motion sickness), and in dogs less than 8 weeks of age for the 2 mg/kg dose (vomiting) as well as in pregnant or lactating bitches. The responsible veterinarian should make a benefit-risk assessment before using Cerenia in dogs under 8 or 16 weeks of age, respectively, or in pregnant or lactating bitches.

Clinical signs including vomiting on first administration, excess salivation and watery faeces have been observed when the product has been overdosed in excess of 20 mg/kg.

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 ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

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

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH 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

Cerenia tablets are supplied in blister packs with four tablets per pack. Not all pack sizes may be marketed.

PACKAGE LEAFLET:
Cerenia 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:

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

Manufacturer responsible for batch release:

FAREVA AMBOISE
Zone Industrielle,
29 route des Industries
37530 Pocé-sur-Cisse
FRANCE

or

Zoetis Manufacturing & Research Spain, S.L.
Ctra. de Camprodón, s/nº
Finca La Riba
Vall de Bianya
Gerona 17813
SPAIN

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cerenia 10 mg/ml solution for injection for dogs and cats
maropitant

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

The solution for injection contains 10 mg maropitant per ml as maropitant citrate monohydrate as a clear, colourless to light yellow solution.
It also contains metacresol (as preservative).

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).

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

Lethargy has been reported in very rare cases, based on post-marketing safety experience.

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, ROUTES AND METHOD OF ADMINISTRATION

For subcutaneous or intravenous use in dogs and cats.

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

In dogs, Cerenia solution for injection can be used to treat or prevent vomiting once daily for up to 5 days.

9. ADVICE ON CORRECT ADMINISTRATION

To prevent vomiting, Cerenia solution for injection should be administered more than 1 hour in advance. The effect duration 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.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE CONDITIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

Shelf life after first opening the vial: 60 days. Do not use this veterinary medicinal product after the expiry date which is stated on the label of the vial after EXP.

12. SPECIAL WARNINGS

Special warnings for each target species:

Vomiting can be associated with serious, severely debilitating conditions and the cause should be investigated. Products such as Cerenia 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. Cerenia should be used with caution in animals suffering from or with predisposition for heart diseases.

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

The efficacy of Cerenia 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 Cerenia 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. The responsible veterinarian should make a benefit-risk assessment before using Cerenia 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:

Cerenia 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, Cerenia solution for injection 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:

Cerenia 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

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH 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

Cerenia 10 mg/ml solution for injection for dogs and cats is available in 20 ml amber glass vials. Each cardboard box contains 1 vial.