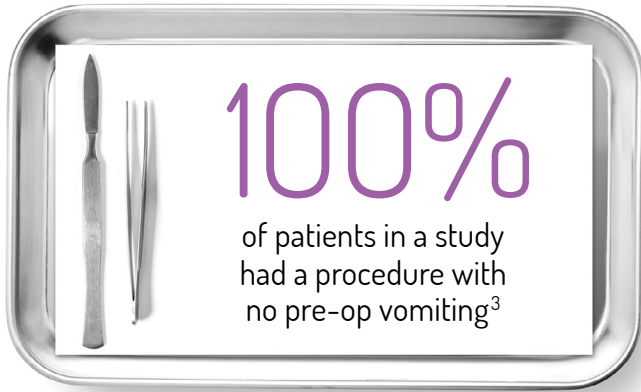


Is Emesis Your Nemesis?

CERENIA® (maropitant citrate) can help your canine patients — and your team — by preventing vomiting due to opioids during spay, neuter, dental and other common procedures.^{1,2}



Research and in-clinic use show that when CERENIA is added to canine preoperative protocols:



of owners would pay for preoperative antiemetic. Fifty-three owners (51.4 %) would definitely and 49 /103 (47.6 %) would probably choose treatment to prevent vomiting (total 99 %).⁴

“When patient calls were done the following day, owners repeatedly said, ‘Thank you! My dog ate!’ This is helping improve relationships between practice and clients as well as owner and pet.”

Adam Christman, DVM
Brick, N.J.

See study results and
read more from your peers:
preventemesis.com

IMPORTANT SAFETY INFORMATION: Use CERENIA Injectable subcutaneously for acute vomiting in dogs 2 to 4 months of age or either subcutaneously or intravenously in dogs 4 months of age and older. Safe use has not been evaluated in cats and dogs with gastrointestinal obstruction, or those that have ingested toxins. Use with caution in dogs with hepatic dysfunction. Pain and vocalization upon injection is a common side effect. In people, topical exposure may elicit localized allergic skin reactions, and repeated or prolonged exposure may lead to skin sensitization. See full Prescribing Information, attached.

*Return to normal feeding was the time at which 100 grams of food was consumed.

1. Data on file, Study Report TI-03333.

2. Study Report No. 1961R-60-11-A81

3. Ramsey D., Fleck T., Berg T. et al. Cerenia prevents perioperative nausea and vomiting and improves recovery in dogs undergoing routine surgery. Inter J Appl Res Vet Med. 2014; 12 (3):229-238.

4. Kraus, BLH, Cazian C. Assessment of dog owner concern regarding peri-operative nausea and vomiting and willingness to pay for anti-emetic treatment. Front Vet Sci. 2019; 6:264

Cerenia[®]

(maropitant citrate)

Tablets and Injectable Solution

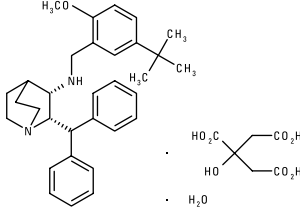
Antiemetic

CERENIA Tablets
For oral use in dogs only
CERENIA Injectable
For subcutaneous or intravenous injection in dogs and cats

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Maropitant is a neurokinin (NK₁) receptor antagonist that blocks the pharmacological action of substance P in the central nervous system (CNS). Maropitant is the non-proprietary designation for a substituted quinuclidine. The empirical formula is C₂₂H₂₆N₂O₃·C₆H₅O₂·H₂O and the molecular weight 678.81. The chemical name is (2S,3S)-2-benzhydryl-N-(5-*tert*-butyl-2-methoxybenzyl)quinuclidin-3-amine citrate monohydrate. Each peach-colored oval tablet is scored and contains 16, 24, 60 or 160 mg of maropitant as maropitant citrate per tablet. Each mL of CERENIA Injectable Solution contains 10 mg maropitant, 63 mg sulphobutylether-beta-cyclodextrin, 3.3 mg meta-cresol and water for injection.

The chemical structure of maropitant citrate is:



INDICATIONS: CERENIA (maropitant citrate) Tablets are indicated for the prevention of acute vomiting and the prevention of vomiting due to motion sickness in dogs. CERENIA (maropitant citrate) Injectable Solution is indicated for the prevention and treatment of acute vomiting in dogs and for the treatment of vomiting in cats.

DOSE AND ADMINISTRATION:

For Prevention of Acute Vomiting (CERENIA Tablets)

For Prevention of Acute Vomiting in dogs 2-7 months of age: Administer CERENIA Tablets orally at a minimum dose of 2 mg/kg (0.9 mg/lb) body weight once daily for up to 5 consecutive days (see WARNINGS and Animal Safety).

For Prevention of Acute Vomiting in dogs 7 months of age and older: Administer CERENIA Tablets orally at a minimum dose of 2 mg/kg (0.9 mg/lb) body weight once daily until resolution of acute vomiting.

If vomiting persists despite treatment, the case should be re-evaluated. CERENIA is most effective in preventing acute vomiting associated with chemotherapy if administered prior to the chemotherapeutic agent.

For prevention of acute vomiting, dispense whole or half tablets in strength(s) that most closely result in a 2 mg/kg dose:

Dog body weight		Number of Tablets		
Pounds	Kilograms	16 mg	24 mg	60 mg
8	4	1/2		
15	8	1		
25	12		1	
50	24		2	
65	30			1
130	60			2

Interchangeable use with CERENIA Injectable Solution for Prevention of Acute Vomiting:

In dogs that are actively vomiting, to ensure that the full initial dose is administered, CERENIA Injectable Solution is recommended at a dose of 1 mg/kg once daily. Thereafter, for the prevention of acute vomiting, CERENIA Tablets at a dose of 2 mg/kg once daily may be used interchangeably with CERENIA Injectable Solution for up to 5 days.

For Prevention of Vomiting Due to Motion Sickness in dogs 4 months and older (CERENIA Tablets)

For Prevention of Vomiting due to motion sickness in dogs 4 months of age and older: Administer CERENIA Tablets orally at a minimum dose of 8 mg/kg (3.6 mg/lb) body weight once daily for up to 2 consecutive days (see WARNINGS and Animal Safety).

Administer CERENIA Tablets a minimum of two hours prior to travel with a small amount of food to mitigate vomiting associated with administration of the dose on an empty stomach; however, refrain from feeding a full meal prior to travel.

Prevention of Vomiting Due to Motion Sickness in Dogs 4 months of age and older:

Dispense whole or half tablets in strengths that most closely result in an 8 mg/kg dose once daily for up to 2 consecutive days:

Dog body weight		Number of Tablets			
Pounds	Kilograms	16 mg	24 mg	60 mg	160 mg
2	1	1/2			
3	1.5		1/2		
4	2	1			
6	3		1		
8	4	2			
13	6		2		
16	7.5			1	
22	10				1/2
33	15			2	
44	20				1
66	30				1 1/2
88	40				2
132	60				3

CERENIA Injectable Solution should not be used interchangeably with CERENIA Tablets for the prevention of vomiting due to motion sickness (8mg/kg).

For Prevention and Treatment of Acute Vomiting in Dogs (CERENIA Injectable):

Dogs 2-4 Months of Age: Administer CERENIA Injectable Solution subcutaneously at 1 mg/kg (0.45 mg/lb) equal to 0.1 mL/kg (0.1 mL/2.2 lb) of body weight once daily for up to 5 consecutive days.

Dogs 4 months of Age and Older: Administer CERENIA Injectable Solution intravenously over 1-2 minutes or subcutaneously at 1 mg/kg (0.45 mg/lb) equal to 0.1 mL/kg (0.1 mL/2.2 lb) of body weight once daily for up to 5 consecutive days.

In dogs that are actively vomiting, it is recommended to initiate treatment with CERENIA Injectable Solution. Thereafter, CERENIA Tablets may be used for the prevention of acute vomiting at 2 mg/kg once daily. (See CERENIA Tablets package insert for complete prescribing information).

For Prevention of Vomiting in Dogs 4 months of Age and Older Caused by Emetogenic Medications or Chemotherapeutic Agents: Administer CERENIA Injectable Solution intravenously over 1-2 minutes or subcutaneously at 1 mg/kg (0.45 mg/lb) of body weight one time, 45-60 minutes prior to use of emetogenic medications or chemotherapeutic agents.

For Treatment of Vomiting in Cats 4 Months of Age and Older (CERENIA Injectable):

Administer CERENIA Injectable Solution intravenously over 1-2 minutes or subcutaneously at 1 mg/kg (0.45 mg/lb) equal to 0.1 mL/kg (0.1 mL/2.2 lb) of body weight once daily for up to 5 consecutive days.

The underlying cause of acute vomiting should be identified and addressed in dogs and cats that receive CERENIA Injectable Solution. If vomiting persists despite treatment, the case should be re-evaluated.

INFORMATION FOR USE: If vomiting persists despite treatment, the case should be re-evaluated. CERENIA is most effective in preventing vomiting associated with chemotherapy if administered prior to the chemotherapeutic agent.

For dogs, CERENIA Injectable Solution may be used interchangeably with CERENIA Tablets for once daily dosing for the prevention of acute vomiting.

WARNINGS: Not for use in humans. Keep out of the reach of children. In case of accidental ingestion, seek medical advice. Topical exposure may elicit localized allergic skin reactions in some individuals. Repeated or prolonged exposure may lead to skin sensitization. Wash hands with soap and water after administering drug. CERENIA is also an ocular irritant. In case of accidental eye exposure, flush with water for 15 minutes and seek medical attention.

In puppies younger than 11 weeks of age, histological evidence of bone marrow hypocellularity was observed at higher frequency and greater severity in puppies treated with CERENIA compared to control puppies. In puppies 16 weeks and older, bone marrow hypocellularity was not observed (see **ANIMAL SAFETY**).

PRECAUTIONS: The safe use of CERENIA Tablets has not been evaluated in dogs or cats used for breeding, or in pregnant or lactating bitches or queens. The safe use of CERENIA Injectable Solution has not been evaluated in dogs or cats with gastrointestinal obstruction or that have ingested toxins.

Use with caution in patients with hepatic dysfunction because CERENIA Injectable Solution is metabolized by CYP3A, CYP2D15 (dogs) and CYP1A (cats) enzymes (see **Pharmacokinetics**). The influence of concomitant drugs that may inhibit the metabolism of CERENIA Injectable Solution has not been evaluated. CERENIA Injectable Solution is highly protein bound. Use with caution with other medications that are highly protein bound. The concomitant use of CERENIA Injectable Solution with other protein bound drugs has not been studied in dogs or cats. Commonly used protein bound drugs include NSAIDs, cardiac, anticonvulsant, and behavioral medications. Drug compatibility should be monitored in patients requiring adjunctive therapy.

CERENIA Tablets causes dose related decreases in appetite and body weight (see **ANIMAL SAFETY**). To maximize therapeutic potential of CERENIA Tablets, the underlying cause of vomiting should be identified and addressed in dogs receiving CERENIA Tablets.

The safe use of CERENIA Injectable Solution has not been evaluated in dogs or cats used for breeding, or in pregnant or lactating bitches or queens.

ADVERSE REACTIONS:

Prevention of Acute Vomiting (minimum of 2 mg/kg) (CERENIA Tablets)

The following adverse reactions were reported during the course of a US field study for the prevention of acute vomiting in dogs treated with CERENIA Tablets at a minimum of 2 mg/kg orally and/or Injectable Solution at 1 mg/kg subcutaneously once daily for up to 5 consecutive days:

Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=69)		CERENIA (n=206)	
	# dogs	% occurrence	# dogs	% occurrence
Death during study	4	5.8	10	4.9
Euthanized during study	0	0	2	1
Diarrhea	6	8.7	4	3.9
Hematochezia/bloody stool	5	7.2	8	1.9
Anorexia	2	2.9	3	1.5
Otitis/Otorrhea	0	0	3	1.5
Endotoxic Shock	1	1.4	2	1
Hematuria	0	0	2	1
Excoriation	0	0	2	1

Other clinical signs were reported but were <0.5% of dogs.

Prevention of Vomiting Due to Motion Sickness (minimum of 8 mg/kg) (CERENIA Tablets)

The following adverse reactions were reported during US studies for the prevention of vomiting due to motion sickness in dogs treated with CERENIA Tablets at a minimum of 8 mg/kg orally one time. Dogs may have experienced more than one of the observed adverse reactions.

Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=195)		CERENIA (n=208)	
	# dogs	% occurrence	# dogs	% occurrence
Hypersalivation	19	9.7	26	12.5
Vomiting ¹	0	0	11	5.3
Muscle Tremors	1	0.5	2	1
Sedation/Depression	3	1.5	2	1
Retching	3	1.5	1	0.5
Flatulence	0	0	1	0.5

¹ Not associated with motion sickness

The following adverse reactions were reported during a European field study for the prevention of vomiting due to motion sickness in dogs treated with CERENIA Tablets at a minimum of 8 mg/kg orally once daily for 2 consecutive days. Dogs may have experienced more than one of the observed adverse reactions.

Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=106)		CERENIA (n=107)	
	# dogs	% occurrence	# dogs	% occurrence
Vomiting	4	4	10	9
Drowsiness/Lethargy/Apathy	1	1	8	8
Hypersalivation	2	2	5	5
Anxiety	0	0	2	2
Trembling/Tremors	0	0	2	2
Inappetence	0	0	2	2
Mucus in stool	0	0	1	1

The following Adverse Reactions were reported during the conduct of a US clinical field trial where CERENIA Tablets were administered once daily for 28 consecutive days to 32 dogs: lethargy, vomiting, inappetence, corneal edema, and enlarged lymph nodes.

Post-Approval Experience (CERENIA Tablets - Revised May 2019)

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events reported for dogs are listed in decreasing order of frequency: anorexia, depression/lethargy, hypersalivation, vomiting, diarrhea, trembling, ataxia, allergic reactions, weight loss, convulsion, hyperactivity, and panting.

Cases of ineffectiveness have been reported.

Cases of death (including euthanasia) have been reported.

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Zoetis Inc. at 1-888-963-8471 or www.zoetis.com.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

(CERENIA Injectable):

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

For a complete listing of adverse reactions for CERENIA Injectable Solution reported to CVM see: <http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055369.htm>

For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Zoetis Inc. at 1-888-963-8471.

DOGS:

In a US field study for the prevention and treatment of vomiting associated with administration of cisplatin for cancer chemotherapy, the following adverse reactions were reported in 77 dogs treated with CERENIA Injectable Solution at 1 mg/kg subcutaneously or 41 dogs treated with placebo:

Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=41)		CERENIA (n=77)	
	# dogs	% occur	# dogs	% occur
Diarrhea	1	2.4	6	7.8
Anorexia	0	0	4	5.2
Injection site reaction (swelling, pain upon injection)	0	0	3	4
Lethargy	1	2.4	2	2.6

The following adverse reactions were reported during the course of a US field study for the prevention and treatment of acute vomiting in dogs treated with 1 mg/kg CERENIA Injectable Solution subcutaneously and/or CERENIA Tablets at a minimum of 2 mg/kg orally once daily for up to 5 consecutive days:

Frequency Distribution of Numbers of Vomiting Episodes
For Treatment: Number of Vomiting Episodes Post Injection.
For Prevention: Total Number of Vomiting Episodes.

Number of Vomiting Episodes	Dogs with Vomiting Episodes* (% of Dogs)			
	Treatment of Vomiting		Prevention of Vomiting	
	Placebo (n=39**)	CERENIA (n=38**)	Placebo (n=41)	CERENIA (n=39)
0	2 (5.1)	8 (21.1)	2 (4.9)	37 (94.9)
1	3 (7.7)	7 (18.4)	2 (4.9)	1 (2.6)
2	4 (10.3)	6 (15.8)	3 (7.3)	1 (2.6)
3	3 (7.7)	6 (15.8)	4 (9.8)	0 (0)
4	4 (10.3)	4 (10.5)	3 (7.3)	0 (0)
5	2 (5.1)	5 (13.2)	4 (9.8)	0 (0)
6	14 (35.9)	1 (2.6)	1 (2.4)	0 (0)
7	2 (5.1)	1 (2.6)	12 (29.3)	0 (0)
8	2 (5.1)	0 (0)	5 (12.2)	0 (0)
9	2 (5.1)	0 (0)	2 (4.9)	0 (0)
10	0 (0)	0 (0)	2 (4.9)	0 (0)
11	1 (2.6)	0 (0)	0 (0)	0 (0)
12	NA	NA	1 (2.4)	0 (0)

*Dogs that exhibited an unacceptable level of vomiting (6 events) were withdrawn from the study and treated with another antiemetic.
 **There were initially 41 and 42 dogs treated with either placebo or CERENIA Injectable Solution, respectively. However, if a dog did not vomit following cisplatin therapy, it did not receive a post-cisplatin treatment with either placebo or CERENIA Injectable Solution, and hence it was not considered in the therapeutic evaluation.

In a study of 275 canine patients presented to veterinary hospitals with a history of acute vomiting, dogs were initially administered CERENIA or placebo on Day 0. Following the initial dose, dogs allocated to the CERENIA group were treated with either CERENIA Tablets at a minimum of 2 mg/kg orally or injectable solution at 1 mg/kg subcutaneously once daily at the discretion of the clinician. Dogs allocated to the placebo group were treated using either an injectable placebo solution or placebo tablets once daily at the discretion of the clinician. Of the 199 dogs included in the analysis for effectiveness, 27 of 54 dogs (50%) in the placebo group displayed vomiting at some time during the study and 31 of 145 dogs (21.4%) in the CERENIA-treated group displayed vomiting during the study period.

Percent of Vomiting for Each Study Day, Based Upon Treatment and Route of Administration.

Days	Treatment	Route	# dogs	# vomited	% vomited
Day 0	Placebo (54)	SC	54	15	28%
	CERENIA (145)	SC	145 (143*)	14	10%
Day 1	Placebo (45)	PO	22	3	14%
		SC	23	16	70%
	CERENIA (108)	PO	67	2	3%
		SC	41	16	39%
Day 2	Placebo (16)	PO	7	2	29%
		SC	9	6	67%
	CERENIA (37)	PO	24	0	0%
		SC	13	8	62%
Day 3	Placebo (6)	PO	2	0	0%
		SC	4	1	25%
	CERENIA (21)	PO	14	0	0%
		SC	7	5	71%
Day 4	Placebo (2)	PO	1	0	0%
		SC	1	1	100%
	CERENIA (7)	PO	5	0	0%
		SC	2	1	50%
Day 5	CERENIA (1)	SC	1	0	0%

*2 dogs administered CERENIA were not observed on Day 0. Their vomiting status was unknown. 143 was used in the denominator for % vomited.

In US field studies in veterinary patients, CERENIA Injectable Solution and Tablets were well tolerated in dogs presenting with various clinical conditions including parvovirus, gastroenteritis, and renal disease. There were no notable differences in mean laboratory values between CERENIA-treated and placebo-treated patients.

CERENIA Injectable Solution was used safely in dogs receiving other frequently used veterinary products such as fluid and electrolyte replacement solutions, antimicrobial agents, vaccines, antacids, and antiparasitic agents.

In a laboratory study, thirty-one dogs were subcutaneously administered CERENIA Injectable Solution or saline, at 1 mL/10 kg body weight, 45 minutes prior to administration of an opioid analgesic. Following administration of the opioid analgesic, none of the CERENIA Injectable Solution treated dogs vomited and 93.8% (15/16) of placebo-treated dogs vomited.

The effectiveness of CERENIA administered at 1 mg/kg IV was demonstrated by bridging the results of a PK study to clinical data supporting effectiveness of 1 mg/kg administered SC. The IV and SC administration of a single dose of 1 mg/kg maropitant are equivalent, based on the bioequivalence of the IV and SC AUC₀₋₂₄ and justification for the therapeutic equivalence of the IV and SC C_{max}.

CATS:

In a field study, 195 cats were presented to veterinary hospitals with a history of vomiting associated with various clinical conditions including gastroenteritis, gastritis, pancreatitis, inflammatory bowel disease, neoplasia, and hepatic lipidosis. Cats were treated with CERENIA Injectable Solution or placebo (in a ratio of 2:1) and observed in the veterinary hospital for 24 hours for the presence of an emetic event(s) defined as the observation of the act of vomiting or the presence of vomitus. Cats could continue antiemetic treatment every 24 hours for up to 5 consecutive days at the discretion of the clinician. Of 165 cats included in the analysis for effectiveness, 2 CERENIA Injectable Solution treated cats (1.8%) vomited 1 time each and 10 placebo-treated cats (18.5%) vomited a total of 15 times in the first 24 hours post treatment.

Percent of Cats Vomiting for Each Study Day by Treatment

Study Day	Treatment	# cats	# vomited	% vomited
Day 0	Placebo	54	10	18.5
	CERENIA	111	2	1.8
Day 1	Placebo	20	4	20.0
	CERENIA	34	1	2.9
Day 2	Placebo	9	2	22.2
	CERENIA	8	0	0.0
Day 3	Placebo	5	0	0.0
	CERENIA	5	0	0.0
Day 4	Placebo	3	0	0.0
	CERENIA	1	0	0.0

The effectiveness of CERENIA administered at 1 mg/kg IV was demonstrated by bridging the results of a PK study to clinical data supporting effectiveness of 1 mg/kg administered SC. The IV and SC administration of a single dose of 1 mg/kg maropitant are equivalent, based on the bioequivalence of the IV and SC AUC₀₋₂₄ and justification for the therapeutic equivalence of the IV and SC C_{max}.

ANIMAL SAFETY: Laboratory and field studies have demonstrated that CERENIA Tablets are well tolerated in dogs after oral administration.

Target Animal Safety Study for Acute Vomiting (CERENIA Tablets)

Fifty six Beagle dogs (28 males and 28 females) approximately 16 weeks of age were administered CERENIA Tablets orally once daily for 15 days at 0, 2, 6, and 10 mg/kg. There were 8 dogs (4 males and 4 females) in the 2 mg/kg group and 16 dogs (8 males and 8 females) in all other groups. CERENIA Tablets caused decreases in food consumption and body weight that were not dose-dependent and did not persist after cessation of treatment.

Beagle dogs approximately 8 weeks of age were administered CERENIA Tablets orally once daily for 15 days at 0, 2, 6, and 10 mg/kg using a protocol similar to the previous study. A dose dependent increase in severity of bone marrow hypoplasia was observed histologically. Interpretation of these study results is complicated by the health status of study animals. Dogs used in the study were weaned early, minimally acclimated to the test facility, many of the dogs in the study tested positive for coccidia and some tested positive for canine parvovirus.

Beagle dogs approximately 10 weeks of age were administered either placebo tablets for 2 days, CERENIA Tablets at 8 mg/kg for 2 days, placebo (saline) subcutaneously (SC) for 5 days, CERENIA Injectable Solution at 1 mg/kg SC for 5 days, or CERENIA Tablets at 2 mg/kg for 5 days (8 dogs in each dose group). Mild pain associated with injection was noted in more dogs and lasted longer in dogs that received maropitant injections compared to saline. Males administered CERENIA at 8 mg/kg orally for 2 days had a decrease in food consumption. Body weight and food consumption were variable throughout the 4 week acclimation period. Two dogs that received 8 mg/kg maropitant orally for 2 days were below the reference range for reticulocyte counts. Decreases in reticulocyte counts were also seen in 4 (of 8) placebo treated dogs (SC saline for 5 days). Hypocellular femoral bone marrow described as "minimal" was seen in 1 male that received 1 mg/kg maropitant SC for 5 days; reticulocyte counts were not available for this dog.

Twenty four Beagle dogs (12 males and 12 females) 7 months of age were administered maropitant at doses of 0, 1, 5, and 20 mg/kg orally once daily for 93 consecutive days. Maropitant produced sporadic clinical signs (salivation, emesis), body weight loss, and lower serum albumin levels at 20 mg/kg/day.

Maropitant increased P-R interval, P wave duration, and QRS amplitude in the 20 mg/kg/day dose group. One female in the 20 mg/kg/day group had increased cellularity of the bone marrow. This female was noted to have lower mean red cell parameters (red blood cell count, hemoglobin, hematocrit) and higher platelet counts and reticulocytes.

Target Animal Safety Study for Motion Sickness (CERENIA Tablets)

Forty Beagle dogs (20 males and 20 females) between 16 – 18 weeks of age were administered CERENIA Tablets orally once daily for 6 days at 0, 8 and 24 mg/kg. There were 16 dogs (8 males and 8 females) in the 0 and 24 mg/kg groups and 8 dogs (4 males and 4 females) in the 8 mg/kg group. At 24 mg/kg, CERENIA Tablets caused decreases in food consumption, with decreases in body weight, liver and testis weight; and an increase in RBC count indicating hemoconcentration, but the effects on feed consumption, body weight, and RBCs did not persist in the post-treatment recovery period (beyond Day 5).

Beagle dogs approximately 8 weeks of age were administered CERENIA Tablets orally once daily for 6 days at 0, 8, and 24 mg/kg using a protocol similar to the previous study. One dog in the 24 mg/kg/day group died of unknown causes on study day 2 and a dose dependent increase in occurrence and severity of bone marrow hypoplasia and lymphoid depletion was observed histologically. Interpretation of these study results is complicated by the health status of study animals. Dogs used in the study were weaned early, minimally acclimated to the test facility, and many of the dogs in the study tested positive for coccidia. Additionally, some dogs in the study tested positive for canine parvovirus, however, clinical parvoviral disease was not definitively diagnosed.

Tolerance Studies (CERENIA Tablets)

Twenty four Beagle dogs (14 males and 10 females) between 11 and 25 weeks of age were administered CERENIA Tablets in 2 phases with 8 dogs per group. In the first phase the dogs were administered 0, 20 or 30 mg/kg orally once daily for 7 days and in the second phase 0, 40, or 50 mg/kg once daily for 7 days. CERENIA Tablets administered at 20 and 30 mg/kg caused occasional vomiting. CERENIA Tablets administered at 40 mg/kg and 50 mg/kg caused clinically relevant signs of weight loss, vomiting, soft stools, weakness, lethargy, salivation and hypokalemia. Additionally, leukopenia characterized by a neutropenia and a trend toward decreasing plasma phosphorus values was seen. Decreased heart rate and prolonged corrected QT intervals were seen in all treatment groups in a dose dependent manner.

Twenty-four Beagle dogs (12 males and 12 females) approximately 28 weeks of age were administered maropitant (mesylate salt) orally once daily for 90 days at 0, 1, 5, and 20 mg/kg. End of study body weights in the 20 mg/kg group were 8-15% lower than baseline body weights.

DOGS (CERENIA INJECTABLE):

Laboratory and field studies have demonstrated that CERENIA Injectable Solution is well tolerated in dogs after subcutaneous administration.

Fifty six Beagle dogs (28 males and 28 females) approximately 16 weeks of age were administered CERENIA Injectable Solution subcutaneously once daily for 15 days at 0, 1, 3, and 5 mg/kg. There were 8 dogs (4 males and 4 females) in the 1 mg/kg group and 16 dogs (8 males and 8 females) in all other groups. The primary treatment-related findings were injection site reactions. Swelling, thickened skin, or pain at one or more of the injection sites on one or more days of the study were observed in 6 of 16 animals treated with 3 mg/kg/day and 5 of 16 animals treated with 5 mg/kg/day. Additionally, the activated partial thromboplastin time (APTT) was prolonged (67.5 seconds, reference range 9-15 seconds) in one male dog in the 1 mg/kg group on study day 15. Relationship of the prolonged APTT to drug administration could not be determined.

Beagle dogs approximately 8 weeks of age were administered CERENIA Injectable Solution subcutaneously once daily for 15 days at 0, 1, 3, and 5 mg/kg using a protocol similar to the previous study. A dose dependent increase in frequency and severity of bone marrow hypoplasia was observed histologically. One placebo-treated dog died on day 14 of the study and was diagnosed with suppurative pancreatitis and esophagitis. Interpretation of the study results is complicated by the health status of study animals. Dogs used in the study were weaned early, minimally acclimated to the test facility, and many of the dogs in the study tested positive for coccidia.

Beagle dogs approximately 10 weeks of age were administered either placebo tablets for 2 days, CERENIA Tablets at 8 mg/kg for 2 days, placebo (saline) subcutaneously (SC) for 5 days, CERENIA Injectable Solution at 1 mg/kg SC for 5 days, or CERENIA Tablets at 2 mg/kg for 5 days (8 dogs in each dose group). Mild pain associated with injection was noted in more dogs and lasted longer in dogs that received maropitant injections compared to saline. Males administered CERENIA Tablets at 8 mg/kg orally for 2 days had a decrease in food consumption. Body weight and food consumption were variable throughout the 4 week acclimatization period. Two dogs that received 8 mg/kg maropitant orally for 2 days were below the reference range for reticulocyte counts. Decreases in reticulocyte counts were also seen in 4 (of 8) placebo treated dogs (SC saline for 5 days). Hypocellular femoral bone marrow described as "minimal" was seen in 1 male that received 1 mg/kg maropitant SC for 5 days; reticulocyte counts were not available for this dog.

Twenty four Beagle dogs approximately 16 weeks of age were administered CERENIA Injectable Solution intravenously once daily for 5 days at 0, 1, and 3 mg/kg (4 females and 4 males per group). CERENIA Injectable Solution was administered at room temperature over 1-2 minutes. Reaction to injection was not specifically recorded. One male dog in the 1 mg/kg group had low hematocrit and white blood cell count on study day 5. One female dog in the 3 mg/kg group had an increased fibrinogen on study day 5. There were no other clinically relevant findings during the study, at necropsy or in histopathology.

CATS (CERENIA INJECTABLE):

Thirty-two domestic short hair cats (16 males and 16 females) approximately 16 weeks of age were administered CERENIA Injectable Solution subcutaneously once daily for 15 days at 0, 1, 3, and 5 mg/kg. There were 8 cats (4 males and 4 females) in each group. Treatment-related, dose dependent findings included pain associated with injection of CERENIA Injectable Solution and injection site heat, pain, redness, and firmness. Pain on injection was observed in 5% of cats at 0 mg/kg, 50% of cats at 1 mg/kg, and 75% of cats at 3 and 5 mg/kg. Injection site firmness >10 mm in diameter was observed at one or more of the injection sites, on one or more days of the study, in 1 of 8 cats at 1 mg/kg, 7 of 8 cats at 3 mg/kg, and 7 of 8 cats at 5 mg/kg. There was a statistically significant reduction (p=0.0171) in food intake as 5 mg/kg compared to cats at 0 mg/kg. One cat at 5 mg/kg was lethargic on Days 12, 13, and 14 of the study. Increased skin turgor was observed in 1 cat at 3 mg/kg on Days 10 and 11, 1 cat at 3 mg/kg on Day 12, and 1 cat at 5 mg/kg on Day 12. At gross necropsy, there were no treatment-related findings. Histopathologic evaluation of injection sites revealed a dose dependent inflammatory response.

Twenty-four healthy domestic shorthair cats (12 males and 12 females) approximately 16 weeks of age were administered maropitant at 1 or 3 mg/kg, or saline at 0.1 mL/kg intravenously once daily for 5 days. CERENIA Injectable Solution was administered at room temperature over 1-2 minutes. Reaction to injection was not specifically recorded, but one cat experienced discomfort with accidental extravascular administration. There were no clinically relevant findings during the study, at necropsy or in histopathology.

STORAGE CONDITIONS:

CERENIA Tablets should be stored at controlled room temperature 20°–25°C (68°–77°F) with excursions between 15°–30°C (59°–86°F). CERENIA Injectable Solution should be stored at controlled room temperature 20-25°C (68-77°F) with excursions between 15-30°C (59-86°F). After first vial puncture, CERENIA Injectable Solution should be stored at refrigerated temperature 2-8°C (36-46°F). Use within 90 days of first vial puncture. Stopper may be punctured a maximum of 25 times.

HOW SUPPLIED:

CERENIA peach-colored tablets are scored with a break line, and contain 16, 24, 60 or 160 mg of maropitant as maropitant citrate per tablet. Each tablet is marked with "MPT" and the tablet strength. Each tablet size is packaged in a bottle containing 60 tablets and packaged in blister packs containing 4 tablets per perforated sheet.

CERENIA Injectable Solution is supplied in 20 mL amber glass vials. Each mL contains 10 mg of maropitant as maropitant citrate.

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