frank:™

CERENIA™ (citrato de maropitant) tabletas:

Pfizer Animal Health Ciencia y experiencia a su servicio

: INFÓRMESE

Asegúrese de leer esta información antes de que su perro reciba Cerenia™. Deberá revisarla también cada vez que su perro reciba una prescripción para este tratamiento.

Esta información es solamente un resumen y no debe reemplazar lo que su veterinario le ha dicho. Para obtener más información sobre Cerenia™, hable con su veterinario.

: ¿QUÉ ES CERENIA™ Y CÓMO FUNCIONA?

Cerenia (citrato de maropitant) es un medicamento antiemético (contra los vómitos) destinado a la prevención de los vómitos en los perros, incluidos los vómitos causados por el mareo con el movimiento.

En todo el cuerpo hay receptores, similares a los interruptores de la luz, que pueden ser estimulados por muchos elementos diferentes causantes de vómitos, como los medicamentos, las toxinas o el movimiento. Estos receptores envían señales al centro de emesis del cerebro. Cerenia funciona bloqueando (inactivando) los receptores del centro de emesis para evitar los vómitos.

: ¿CUÁNDO DEBE USARSE CERENIA™ EN LOS PERROS?

En presencia de vómitos agudos, y antes de prescribir Cerenia™, su veterinario verificará que no haya trastornos médicos primarios graves que necesiten un tratamiento más específico.

En el caso de perros sanos con antecedentes de mareos por movimiento, Cerenia™ puede administrarse 2 horas antes de viajar para ayudar a evitar el signo típico de vómitos.

: ¿CÓMO SE ADMINISTRA CERENIA™ A LOS PERROS?

Cerenia es una tableta que se administra al perro por la boca. También está disponible en forma de inyección que su veterinario puede administrarle al perro en la clínica.

Siempre siga las instrucciones de su veterinario cuando administre Cerenia en su casa.

: ¿CÓMO SE USA CERENIA™ PARA EVITAR LOS VÓMITOS AGUDOS?

Su veterinario puede prevenir los vómitos agudos prescribiendo Cerenia™ en combinación con otras medidas, por ejemplo, no ofreciendo alimentos o efectuando cambios en la dieta. Cerenia™ puede administrarse hasta por 5 días para la prevención de los vómitos agudos.

: ¿CÓMO PUEDO ADMINISTRAR CERENIA™ A MI PERRO PARA EVITAR EL MAREO POR MOVIMIENTO?

Cerenia da los mejores resultados cuando se administra 2 horas antes de viajar. Como cualquier otro medicamento, Cerenia no ofrece un 100% de eficacia, de modo que algunos perros todavía pueden presentar algunos signos de mareo por movimiento,

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CERENIA™ (citrato de maropitant) tabletas:

como babeo excesivo y vómitos, a pesar del tratamiento preventivo.

Antes de administrar el medicamento para evitar el mareo por movimiento, se recomienda ofrecer una comida liviana o un bocado. Sin embargo, las tabletas de Cerenia no deben envolverse ni encapsularse en alimentos, porque tal medida puede interferir en la disolución de la tableta de Cerenia y demorar su efecto.

La dosis de Cerenia administrada para impedir el mareo por movimiento es mayor que la dosis usada para evitar los vómitos agudos, de modo que Cerenia puede usarse por un máximo de dos días consecutivos para evitar el mareo por movimiento.

: ¿CERENIA™ TIENE EFECTOS SECUNDARIOS?

En los estudios realizados con Cerenia™, los efectos secundarios fueron infrecuentes, pero comprendieron diarrea, heces sanguinolentas, pérdida del apetito, babeo, vómitos o arcadas, temblores musculares, flatulencia, inflamación en los oídos y muerte. Algunos de los perros inscritos en los estudios clínicos realizados con Cerenia para los vómitos debidos a enfermedad médica, estaban muy enfermos y presentaban trastornos potencialmente mortales. Un porcentaje reducido de estos perros murieron durante el estudio (5,8% en el grupo que recibió placebo [no tratados] y 4,9% en el grupo tratado con Cerenia). Se cree que las muertes fueron causadas por la enfermedad o el trastorno primario causante de los vómitos en el animal y no debido a Cerenia. En este momento, no hay evidencia directa que vincule estas muertes al uso de Cerenia.

Llame a su veterinario si observa cualquier cambio en su mascota mientras toma Cerenia™.

: ¿HAY PERROS QUE NO DEBAN RECIBIR CERENIA™?

Cerenia™ debe administrarse a perros sanos.

El uso en animales en cría, preñadas o lactantes no ha sido evaluado. El uso en animales con obstrucción GI o perros que hayan ingerido toxinas no ha sido evaluado.

Cerenia™ se usó sin peligros en combinación con muchos otros medicamentos veterinarios comunes. Informe siempre a su veterinario si su perro está tomando otros medicamentos.

Usar con cautela en perros con trastornos del hígado.

Cerenia se recomienda para usarse en perros a partir de 16 semanas.

: ¿QUÉ MÁS DEBO SABER ACERCA DE CERENIA™?

Asegúrese de informar a su veterinario si su perra está preñada o lactando, o si está planificando su reproducción.

Cerenia™ debe usarse solamente en perros.

Como sucede con cualquier medicamento, Cerenia™ debe mantenerse fuera del alcance de los niños y las mascotas.

Un elemento educativo ofrecido por Pfizer Animal Health

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Cerenia™ (maropitant citrate)

Tablets and Injectable Solution

Antiemetic

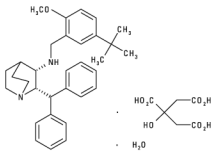
CERENIA Tablets
For oral use in dogs only

CERENIA Injectable
For subcutaneous injection in dogs only

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

DESCRIPTION: Maropitant is a neurokinin (NK_1) 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 $C_{29}H_{40}N_2O \cdot C_6H_8O_7 \cdot H_2O$ and the molecular weight 678.81. The chemical name is (2*S*,3*S*)-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 metacresol 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 Injectable Solution is indicated for the prevention and treatment of acute vomiting in dogs.

DOSAGE AND ADMINISTRATION: CERENIA Tablets and CERENIA Injectable Solution are recommended for use in dogs 16 weeks and older.

For Prevention of Acute Vomiting (CERENIA Tablets)
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.

Prevention of Acute Vomiting
Minimum of 2 mg/kg BW Dosing

Dog body weight		Number of Tablets		
Pounds	Kilograms	16 mg	24 mg	60 mg
2.2 – 8.8	1.0 – 4.0	1/2		
8.9 – 17.6	4.1 – 8.0	1		
17.7 – 26.4	8.1 – 12.0		1	
26.5 – 52.8	12.1 – 24.0		2	
52.9 – 66.0	24.1 – 30.0			1
66.1 – 132.0	30.1 – 60.0			2

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

For Prevention of Vomiting Due to Motion Sickness (CERENIA Tablets)
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. Dogs should be fasted 1 hour prior to administration of CERENIA Tablets. Administer CERENIA Tablets 2 hours prior to travel.

Prevention of Vomiting due to Motion Sickness
Minimum of 8 mg/kg BW Dosing

Dog body weight		Number of Tablets			
Pounds	Kilograms	16 mg	24 mg	60 mg	160 mg
2.2	1	1/2			
2.3 – 3.3	1.1 – 1.5		1/2		
3.4 – 4.4	1.6 – 2.0	1			
4.5 – 6.6	2.1 – 3.0		1		
6.7 – 8.8	3.1 – 4.0	2			
8.9 – 13.2	4.1 – 6.0		2		
13.3 – 16.5	6.1 – 7.5			1	
16.6 – 22.0	7.6 – 10.0				1/2
22.1 – 33.0	10.1 – 15.0			2	
33.1 – 44.0	15.1 – 20.0				1
44.1 – 66.0	20.1 – 30.0				1 1/2
66.1 – 88.0	30.1 – 40.0				2
88.1 – 132.0	40.1 – 60.0				3

For Prevention and Treatment of Acute Vomiting (CERENIA Injectable Solution)
Administer CERENIA Injectable Solution subcutaneously at 1.0 mg/kg (0.45 mg/lb) equal to 1.0 mL/10 kg (1.0 mL/22 lb) of body weight once daily for up to 5 consecutive days.

Dog body weight		Dose Volume (mL)
Pounds	Kilograms	
2.2	1.0	0.10
2.3 – 4.4	1.1 – 2.0	0.20
4.5 – 6.6	2.1 – 3.0	0.30
6.7 – 8.8	3.1 – 4.0	0.40
8.9 – 11.0	4.1 – 5.0	0.50
11.1 – 16.5	5.1 – 7.5	0.75
16.6 – 22.0	7.6 – 10.0	1.00
22.1 – 33.0	10.1 – 15.0	1.50
33.1 – 44.0	15.1 – 20.0	2.00
44.1 – 66.0	20.1 – 30.0	3.00
66.1 – 88.0	30.1 – 40.0	4.00
88.1 – 110.0	40.1 – 50.0	5.00
110.1 – 132.0	50.1 – 60.0	6.00

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, injection or exposure, 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 or accidental skin exposure. 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 hypoplasia was seen at higher frequency and greater severity in puppies treated with CERENIA than in control puppies. In puppies 16 weeks and older, bone marrow hypoplasia was not seen (See Animal Safety Section).

PRECAUTIONS: CERENIA Injectable Solution is for subcutaneous injection only. The safe use of CERENIA Tablets and CERENIA Injectable Solution have not been evaluated in dogs used for breeding, pregnant or lactating bitches, dogs with gastrointestinal obstruction, or dogs that have ingested toxins. Use with caution in dogs with hepatic dysfunction. Use with caution with other medications that are highly protein bound. The concomitant use of CERENIA with other protein bound drugs has not been studied in dogs. Commonly used protein bound drugs include NSAIDs, cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of CERENIA has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

ADVERSE REACTIONS:
Prevention of Acute Vomiting (minimum of 2 mg/kg)
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 1.0 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	1.0
Diarrhea	6	8.7	8	3.9
Hematochezia/bloody stool	5	7.2	4	1.9
Anorexia	2	2.9	3	1.5
Otitis/Otorrhea	0	0	3	1.5
Endotoxic Shock	1	1.4	2	1.0
Hematuria	0	0	2	1.0
Excoriation	0	0	2	1.0

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

Prevention of Vomiting Due to Motion Sickness (minimum of 8 mg/kg)
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	1.0
Sedation/Depression	3	1.5	2	1.0
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

Prevention and Treatment of Acute Vomiting (1 mg/kg)
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 1.0 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**	**4.0**
Lethargy	**1**	**2.4**	**2**	**2.6**

Adverse reactions seen in a European field study included ataxia, lethargy and injection site soreness in one dog treated with CERENIA Injectable Solution.

For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Pfizer Animal Health at 1-800-366-5288.

CLINICAL PHARMACOLOGY: Pharmacokinetics

The pharmacokinetic characterization associated with maropitant after oral (PO) or subcutaneous (SC) administration in adult Beagle dogs is provided in the table below.

Pharmacokinetic Parameters in Beagle Dogs (Mean±SD or range)			
	SC at 1 mg/kg (n=6)	PO at 2 mg/kg (n=8)	PO at 8 mg/kg (n=8)
$AUC_{0\text{-}inf}$ (hr*ng/mL)	860±137	561±322	7840±5600
C_{max} (ng/mL)	92±34	81±32	776±604
$T_{1/2}$ (hr)	8.84 (6.07-17.7)	4.03 (2.48-7.09)	5.46 (3.39-7.65)
T_{max} (hr)	0.75±1.11	1.9±0.5	1.7±0.7

The absolute bioavailability of maropitant was much higher following SC injection (91% at 1 mg/kg) than after PO administration (24% at 2 mg/kg). Oral bioavailability may be underestimated due to the presence of nonlinear kinetics and the resulting longer $T_{1/2}$ seen after intravenous (IV) administration. Although hepatic first-pass metabolism contributed to the relatively low bioavailability after an oral dose, prandial status does not significantly affect the extent of oral bioavailability. Greater than dose-proportional drug exposure can be expected with an increase in dose (1-16 mg/kg PO). Systemic clearance of maropitant following IV administration was 970, 995, and 533 mL/hr/kg at doses of 1, 2 and 8 mg/kg, respectively. An accumulation ratio of 1.5 was observed following once-daily use of maropitant for five consecutive days at 1 mg/kg (SC) or 2 mg/kg (PO). Urinary recovery of maropitant and its major metabolite was minimal (<1% each). The hepatic metabolism of maropitant involves two cytochrome P-450 isoenzymes: CYP2D15 and CYP3A12. Based on *in vitro* enzyme kinetics data, it is believed that the non-linear kinetics may be partially associated with saturation of the low capacity enzyme (CYP2D15). However as doses increase (20-50 mg/kg PO), dose proportionality is re-established. Based upon *in vitro* enzyme kinetics, involvement of a high capacity enzyme (CYP3A12) may contribute to this return to dose linearity. Plasma protein binding of maropitant was high (99.5%).

Pharmacodynamics
Vomiting is a complex process coordinated centrally by the emetic center which 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 (NK_1) receptor antagonist which acts by inhibiting the binding of substance P, a neuropeptide of the tachykinin family. Substance P is found in significant concentrations in the nuclei comprising the emetic center and is considered the key neurotransmitter involved in emesis.[2] By inhibiting the binding of substance P within the emetic center, maropitant provides broad-spectrum effectiveness against neural (central) and humoral (peripheral) causes of vomiting. *In vivo* model studies in dogs have shown that maropitant has antiemetic effectiveness against both central and peripheral emetogens including apomorphine, and syrup of ipecac.

[2]Diemunsch P, Grelot L. Potential of substance P antagonists as antiemetics. [Review] [60 refs]. Drugs. 2000;60:533-46.

EFFECTIVENESS:
Prevention of Acute Vomiting
In laboratory model studies, CERENIA Tablets dosed at a minimum of 2 mg/kg BW reduced the number of emetic events associated with established neural (central) and humoral (peripheral) stimuli. Following administration of apomorphine (central emetic stimuli), vomiting was observed in 33% (4 of 12) of Beagle dogs treated with CERENIA Tablets and 100% (12 of 12) of Beagle dogs treated with placebo tablets. Following administration of syrup of ipecac (peripheral emetic stimuli) vomiting was observed in 33% (4 of 12) of Beagle dogs treated with CERENIA Tablets and in 83% (10 of 12) of Beagle dogs treated with placebo tablets.

In a study of 275 canine patients presented to veterinary hospitals with a history of acute vomiting, dogs were initially administered CERENIA Injectable Solution 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 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.

Prevention of Vomiting due to Motion Sickness
In a study of canine veterinary patients taken on a one-hour car journey and treated with either CERENIA Tablets at a minimum dose of 8 mg/kg BW or placebo tablets 2 hours prior to the journey, 67 of 122 (55%) of dogs vomited during the journey when treated with placebo while 8 of 122 (7%) vomited during the journey after treatment with CERENIA Tablets. The probability that a dog in this study, prone to motion sickness would NOT vomit during a journey if treated with CERENIA Tablets was 93%, while the probability was 48% if treated with placebo.

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Prevention and Treatment of Acute Vomiting (CERENIA Injectable Solution)
In laboratory model studies, CERENIA Injectable Solution administered at 1 mg/kg in Beagle dogs reduced the number of emetic events associated with established neural (central) and humoral (peripheral) stimuli. Following administration of apomorphine (central emetic stimuli), vomiting was observed in 16.7% (2 of 12) of dogs treated with CERENIA Injectable Solution and 83.3% (10 of 12) of placebo-treated dogs. Following administration of syrup of ipecac (peripheral emetic stimuli) vomiting was observed in 25% (3 of 12) of dogs treated with CERENIA Injectable Solution and in 100% (12 of 12) of dogs treated with placebo.

In a study of veterinary cancer patients, dogs were treated with CERENIA Injectable Solution or placebo either 1 hour prior to cisplatin (prevention) or after the first vomiting episode following cisplatin (treatment) and monitored for 5 hours. In the groups evaluated for prevention of vomiting, 94.9% (37/39) of the dogs administered CERENIA Injectable Solution and 4.9% (2/41) of the dogs administered placebo did not vomit. In the groups evaluated for treatment, 21% (8/38) of the dogs administered CERENIA Injectable Solution and 5.1% (2/39) of the dogs administered placebo had no further episodes of vomiting following treatment.

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, and hence it was not considered in the therapeutic evaluation.

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

Target Animal Safety Study for Acute Vomiting
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.

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 was 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.

Target Animal Safety Study for Motion Sickness
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 Study
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.

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

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

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). Use within 28 days of first vial puncture.

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 on one side and the Pfizer logo on the other. Each tablet size is 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.

US Patents: See US 6,222,038; US 6,255,320
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