

PREVENTION AID

Maropitant can be an effective antiemetic in felines and is also useful as an adjunct to therapy for visceral pain.

FOCUS ON

Maropitant Use in Cats

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Maropitant, in oral and injectable forms, is commonly used in clinical practice as an antiemetic for feline patients. This article reviews the pharmacokinetics and pharmacodynamics of maropitant and summarizes recent literature for various clinical applications in cats.

MECHANISM OF ACTION

The antiemetic properties of maropitant are attributable to its antagonism of neurokinin-1 receptors and subsequent blockage of the pharmacologic action of substance P. Substance P is a tachykinin that is upregulated in disease processes and plays a role in eliciting emesis as well as in processes such as pain and inflammation.^{1,2} The pathophysiology of vomiting (**FIGURE 1**) involves 2 major areas in the central nervous system—the chemoreceptor trigger zone (CRTZ) and the vomiting center—in addition to afferent signals to and efferent signals from the gastrointestinal tract. The CRTZ is located outside the blood–brain barrier and is stimulated by circulating emetogenic substances (uremic toxins, other toxins, drugs). The vomiting center receives input from the CRTZ as well as the gastrointestinal tract, the vestibular apparatus (vomiting associated with motion sickness), and the cerebral cortex (psychogenic vomiting). Neurokinin-1 receptors are present in the central nervous system (in the CRTZ and the vomiting

center) as well as in the gastrointestinal tract; therefore, maropitant provides widespread blockade of receptors associated with emetic stimuli.^{1,2} In addition, neurokinin-1 receptors and substance P are widespread in pain pathways but are specifically present in a large number of visceral afferents, suggesting that maropitant could play a role in visceral analgesia.²

DOSING

Injectable maropitant is approved for the treatment of vomiting in cats, administered at a dose of 1 mg/kg IV or SC q24h for 5 days. According to a published study, oral maropitant is commonly used off label in cats at the same dose (1 mg/kg q24h), which differs from the labeled dose for dogs (2 mg/kg), probably due to the difference in bioavailability (cats 50% versus dogs 23.7%).¹

PHARMACOKINETICS

The pharmacokinetic properties of maropitant in cats have been described for PO, SC, and IV administration.¹ With all forms of administration, the terminal half-life is 13 to 17 hours. Bioavailability after PO administration is 50% and after SC administration is 117%.¹

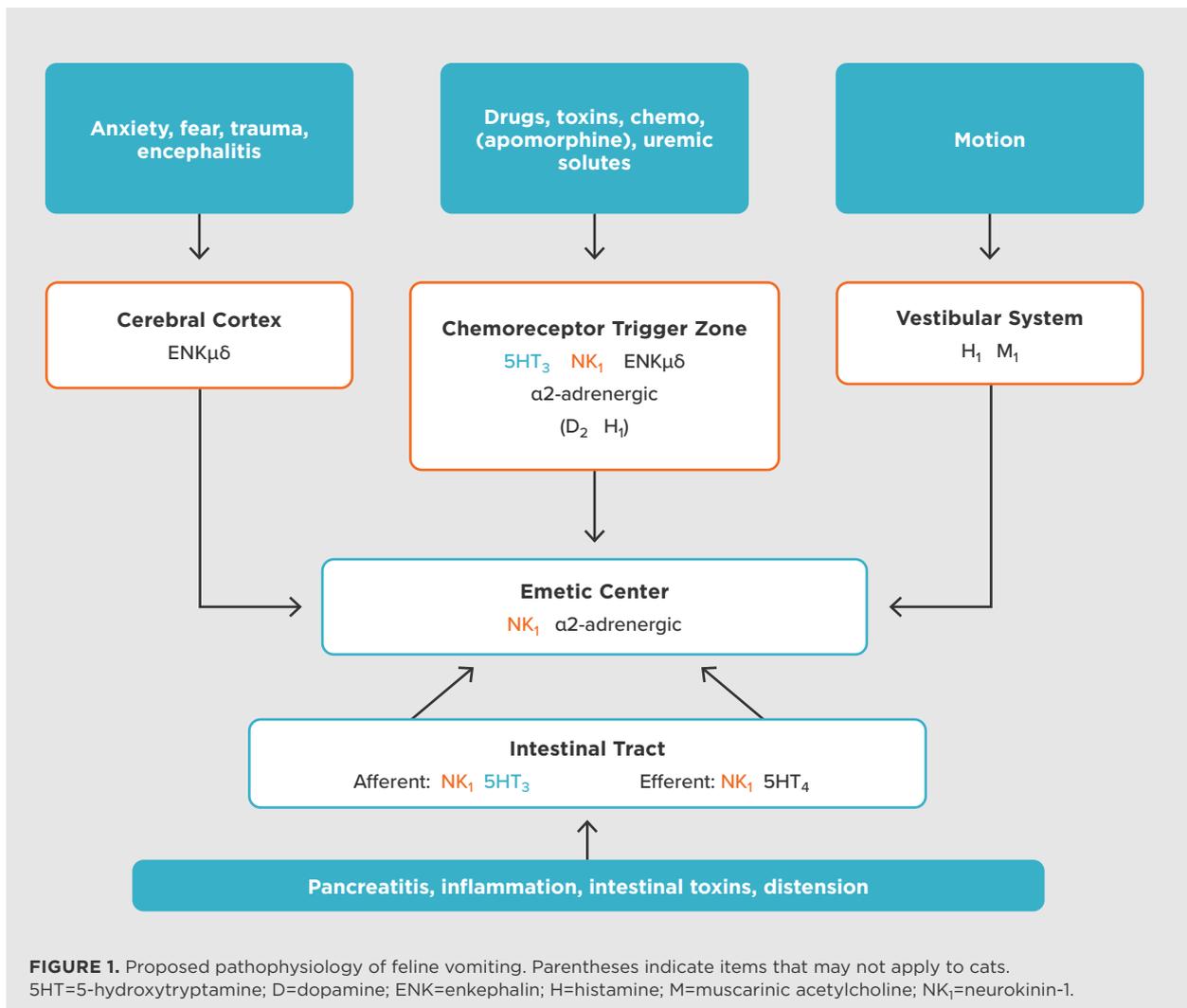
COMMON INDICATIONS

Vomiting

Maropitant has been shown to be an effective antiemetic in cats, ameliorating xylazine-induced vomiting when given PO, SC, or IV.¹ When administered PO or SC at 1 mg/kg 2 hours before administration of xylazine, maropitant significantly reduced the mean number of emetic events by 90% (PO) or 76% (SC). When maropitant was administered IV at 1 mg/kg, emesis was completely prevented. Placebo-controlled assessment of duration showed that maropitant administration 24 hours before xylazine challenge significantly reduced the mean number of emetic events (by 66%) as well as mean visual analog nausea scores.¹

Motion Sickness

When assessed in a laboratory model, maropitant at 1 mg/kg SC was effective against motion-induced vomiting.¹ In a crossover placebo-controlled study, cats determined to be susceptible to motion sickness received either 1 mg/kg maropitant SC or saline placebo and 4 hours later were placed in a motorized device resembling a Ferris wheel for 30 minutes. No emesis occurred when the cats received maropitant during the challenge; in contrast, 1 to 4 emetic events occurred when they received placebo. Motion-induced nausea scores were also significantly decreased when the cats received maropitant.¹ However, nonproductive retching tended to be exhibited more often when the cats received maropitant than when they received placebo, which may be a manifestation of inhibited emesis. Data on the efficacy of maropitant administered PO for motion sickness are not available.



Perioperative Use

A growing body of literature demonstrates that maropitant is useful when given during the perioperative period, both to prevent emesis associated with premedication and as an adjunct analgesic for visceral pain.³⁻⁷ Several studies have assessed the use of maropitant to prevent emesis associated with morphine and dexmedetomidine premedication.⁴⁻⁶ In a crossover blinded study in which maropitant (1 mg/kg) or saline placebo was administered SC 20 hours before premedication, vomiting decreased significantly in cats given maropitant (1/32 cats, 3%) compared with cats given placebo (20/34 cats, 56%).⁵ Retching also decreased significantly in cats given maropitant (6/32 cats, 19%) compared with cats given placebo (20/34, 59%). Signs of nausea (defined as excessive lip licking, or sialorrhea) were somewhat decreased, but the decrease did not reach statistical significance. However, substantial behavioral reactions were seen in response to SC administration of maropitant. As a result, the same research group subsequently performed studies with maropitant administered orally, and results were similar.^{4,6} When maropitant (8 mg/cat PO) was administered either 2 to 2.5 hours or 24 hours before premedication, incidence of vomiting and retching was significantly decreased but not entirely prevented. Some signs of nausea also decreased; however, sialorrhea after oral maropitant administration was observed in a large number of cats. Sialorrhea could also be a result of oral administration, confounding its interpretation as a sign of nausea.

Maropitant has also been demonstrated to be useful for minimizing visceral pain associated with ovariohysterectomy.^{3,7} A study assessing the effect of maropitant on minimum alveolar concentration (MAC) of sevoflurane required for pain control during ovarian ligament stimulation found that when maropitant was administered at 1 mg/kg IV, the sevoflurane MAC required decreased by 15%.⁷ No additional decrease in required sevoflurane MAC was found at a 5 mg/kg IV dose of maropitant. The effect of maropitant (1 mg/kg IV plus continuous rate infusion at 30 µg/kg/hour or 100 µg/kg/hour) during anesthesia for ovariohysterectomy has also been assessed.³ Cats that received the 100 µg/kg/hour protocol had lower Doppler blood pressure and heart rate during the procedure and required fewer postoperative analgesic rescue doses than did cats that received placebo or cats who received the 30 µg/kg/hour infusion.

Chronic Disease

Although maropitant is commonly used for acute vomiting, a pharmacokinetic and toxicity study in cats indicated that longer term use seems to be safe,¹ and maropitant is often used for long-term therapy in chronically ill patients. Anecdotally, long-term use in chronically ill patients seems to be well tolerated. Because of the caution on the package insert for maropitant use in cats with hepatic disease, the dose is often reduced for these patients (usually by 50%), but to date, no specific data about pharmacokinetics in feline patients with hepatic dysfunction have been published. Maropitant may be particularly useful in cats with chronic kidney disease because the drug targets receptors in the CRTZ and vomiting center in the brain, where uremic toxins are sensed, and also targets receptors in the gastrointestinal tract. In a placebo-controlled blinded study in which maropitant was administered daily for 2 weeks at a dose of 4 mg/cat PO to cats with International Renal Interest Society stage 2 and 3 chronic kidney disease, vomiting decreased significantly.⁸

ADVERSE EFFECTS

The most commonly reported adverse effect of injectable maropitant in cats is pain/reaction to SC injection.^{2,5} It seems that local irritation and injection pain are associated with the amount of unbound maropitant in the injection, a phenomenon that is altered by temperature.⁹ When refrigerated, more maropitant is bound and reaction to injection is less. Other adverse effects seem to be minimal. In a safety study assessing injectable maropitant, doses up to 5 mg/kg SC were administered q24h for 15 days, and no adverse effects were noted by physical examination or clinicopathologic assessment. Histopathology indicated inflammation and fibrosis at the injection site.¹ Maropitant is highly protein-bound; thus, without the benefit of studies of drug–drug interactions, concomitant administration of maropitant with other highly protein-bound drugs should be done with caution. For humans administering maropitant, washing hands after handling is advised because maropitant may cause an allergic skin reaction.

SUMMARY

Maropitant is an effective antiemetic in felines and is also useful as an adjunct to therapy for visceral pain. The extent to which maropitant addresses nausea and active emesis is unclear. Longer-term administration for

chronic disease has become more prevalent and seems to be beneficial. Adverse effects seem to be minimal, and the main concern of discomfort from injection can be palliated by keeping the medication cold. **TVP**

Adapted from Washabau RJ. Difficult Vomiting Disorders: Therapy. WSAVA Proc 2009.

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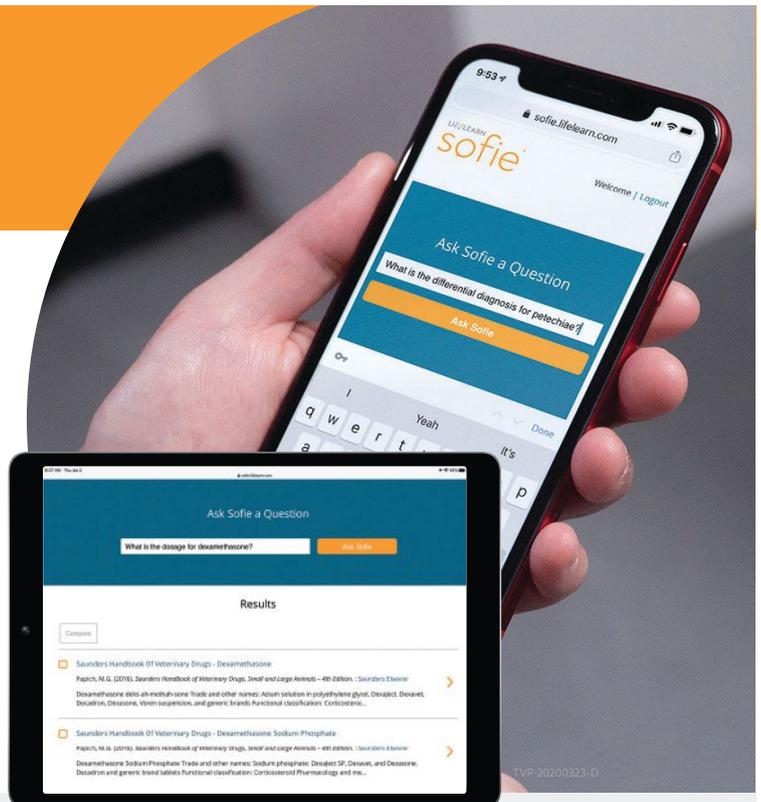
Dr. Quimby is board-certified in small animal internal medicine and completed a PhD studying chronic kidney disease in cats. She was on faculty at Colorado State University until 2017. She is now an associate professor of small animal internal medicine at the Ohio State University. Current research areas include renal pathophysiology, novel treatment strategies, and evidence-based supportive care strategies. She has an interest in feline clinical pharmacology with a focus on improving supportive care and quality of life in cats with chronic kidney disease. Dr. Quimby has received the International Renal Interest Society Award and the AVMF/Winn Feline Foundation Research Award for her contributions to nephrology and feline medicine.

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