

# Maropitant: Novel Antiemetic

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Vomiting can lead to dehydration, weight loss, reflux esophagitis, or aspiration pneumonia. Antiemetics reduce the frequency of vomiting and make patients more comfortable. Vomiting severe enough to warrant an antiemetic should also prompt a reasonable evaluation to look for serious underlying disease, including an abdominal radiograph to assist in ruling out GI obstruction.

Administration of antiemetics empirically in animals with unrecognized GI obstruction can delay diagnosis and potentially worsen prognosis. If vomiting is severe or persistent, CBC, chemistry panel, and a pancreatic lipase test are indicated. Repeated dosing of antiemetics should be avoided unless patients have had this baseline completed. If intestinal obstruction is noted, antiemetics without prokinetic properties can be continued while surgery is planned.

## Maropitant & Its Actions

One of the most effective veterinary antiemetics is maropitant (cerenia.com). It is the first veterinary neurokinin-1 (NK-1) receptor antagonist and inhibits binding of substance P to NK-1 receptors. Substance P is an emetogen experimentally, and is found endogenously, along with NK-1 receptors, in the emetic center, chemoreceptor trigger zone, and in vagal afferent nerves in the gastrointestinal tract.<sup>1</sup>

Because of the wide distribution of substance P, maropitant has efficacy against a broad range of emetic stimuli that act centrally in the brainstem or peripherally in the GI tract. In contrast, ondansetron is primarily effective for peripheral emetic stimuli, while metoclopramide and chlorpromazine are primarily effective for central emetic stimuli.<sup>2</sup> The efficacy of maropitant is highlighted by its ability to prevent emesis in cats induced by xylazine<sup>3</sup> and in dogs induced by syrup of ipecac and apomorphine.<sup>2</sup>

## Indications & Efficacy

Maropitant can be used whenever an antiemetic is indicated and is more effective as a sole agent than metoclopramide in field trials.<sup>4</sup> It has demonstrated efficacy in dogs for vomiting from multiple causes, including dietary indiscretion, pancreatitis, parvoviral enteritis, and nonspecific gastritis.<sup>5</sup> Only 1 or 2 administrations of maropitant were necessary to achieve efficacy in these studies.

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## Chemotherapy

NK-1 antagonists have become the standard of care in human and veterinary cancer patients to prevent vomiting associated with chemotherapy. This may improve quality of life during treatment, prevent expensive hospitalization, and decrease the need for chemotherapy dose reductions. Maropitant is effective in preventing cisplatin-associated vomiting in dogs when administered 1 hour before SC infusion.<sup>6</sup>

Maropitant also significantly decreases the incidence and severity of delayed vomiting (and diarrhea) following doxorubicin treatment when given orally at home for 5 days after treatment; however, nausea and inappetence can still occur.<sup>7</sup>

## Motion sickness

Maropitant is approved by the FDA for prevention of motion sickness in dogs and has proven efficacy for motion sickness in cats.<sup>3</sup> This is an attractive alternative to drugs such as dimenhydrinate and acepromazine, which can cause sedation.

Maropitant can also prevent nausea and vomiting in dogs associated with opioids, such as hydromorphone premedication and epidural morphine.<sup>8,9</sup>

## Pharmacokinetics & Dosing

Maropitant has an elimination half-life of approximately 4 to 8 hours in dogs, with a 24-hour duration of effect. The dosage of maropitant by SC route is 1 mg/kg q24h in dogs. For prevention of vomiting, SC maropitant should be administered for at least 1

continues



### Potential Indications for Maropitant

Substance P is involved in pain pathways, and NK-1 antagonists may have visceral analgesic effects in some species. For example, maropitant has an anesthetic-sparing effect during ovarian manipulation in dogs and cats undergoing ovariohysterectomy, when given at 1 mg/kg IV (followed by a 30 µg/kg/hr CRI in dogs).<sup>18,19</sup> However, in both dogs and cats, transient hypotension (a decrease of 10–30 mm Hg) was noted after the IV bolus.

Substance P has also been implicated in bladder hyperalgesia and airway hyperreactivity. In fact, NK-1 receptor antagonists have demonstrated efficacy in human patients with overactive bladders<sup>20</sup> and in animal models of allergic bronchial disease<sup>21</sup> and induced cough.<sup>22</sup> Additional studies are needed to determine whether maropitant or other drugs in this class are useful in veterinary patients for indications other than the control of vomiting.

hour before anesthesia or chemotherapy; IV administration is reportedly well tolerated but is not approved on the label.<sup>10</sup> Oral dosing is higher (2 mg/kg PO q24h) because of incomplete oral bioavailability. Food does not affect oral drug absorption.

Maropitant is biotransformed in dogs by the cytochrome P450 enzymes CYP3A12 and CYP2D15. Label dosing is limited to 5 consecutive days followed by a 2-day rest period. This is because clearance of maropitant by CYP2D15 becomes saturated at higher drug concentrations.<sup>11</sup> The 2-day rest period prevents accumulation of high drug concentrations during chronic administration. However, maropitant has been administered safely to beagles at 2 mg/kg PO for 2 weeks, without clinical toxicity.<sup>12</sup> Maropitant has minimal renal clearance, suggesting that dosage adjustments are probably not necessary in renal failure.

A much higher dose (8 mg/kg PO q24h) is indicated for motion sickness in dogs, and fasting for 1 hour is recommended before oral administration at this dosage. The drug should be administered 1–2 hours before travel, and lasts at least 11 hours.<sup>11,13</sup> This higher dose is label-approved for a duration of only 2 days because of increased plasma concentrations that accumulate from P450 saturation.<sup>14</sup> In fact, the half-life of maropitant is prolonged to about 22 hours at this dose.<sup>12</sup> Despite drug accumulation, however, no overt toxicity was noted in beagles dosed at 8 mg/kg PO for 14 days.<sup>12</sup> It is not clear whether this would be tolerated in most clinical patients.

In cats, maropitant has a half-life of 13–17 hours, and is cleared more slowly than in dogs.<sup>2</sup> Maropitant is approved in cats at a dosage of 1 mg/kg SC q24h for acute vomiting. The oral tablets are also commonly prescribed to cats off-label, for example, in treating chronic vomiting in cats with chronic renal failure.<sup>15</sup> Maropitant is effective in cats even when given a full 24 hours before emetic challenge.<sup>2</sup>

### Adverse Effects & Contraindications

Adverse effects of maropitant appear to be uncommon at the label dosages. The subcutaneous route can be painful, but refrigeration of the drug vial decreases pain on administration.<sup>16</sup> The drug is not approved for puppies younger than 8 weeks of age or kittens less than 16 weeks of age. The higher dose for motion sickness is approved only for puppies 16 weeks or older. This is because bone marrow hypoplasia was observed in 8-week-old puppies dosed at 6–10 mg/kg/day.<sup>17</sup>

Because maropitant undergoes hepatic clearance, its use should be avoided in patients with hepatic dysfunction.

Maropitant is also highly protein bound, so interactions with other highly protein bound drugs, such as benzodiazepines and some NSAIDs, are possible with acute dosing. Maropitant and other antiemetics should not be used in patients suspected of toxin ingestion, as this may mask progression and allow more time for toxin absorption. In addition, the use of these antiemetics should be delayed until a clinical examination and abdominal radiographs have ruled out GI obstruction.

Maropitant can be used in combination with other antiemetics, for example metoclopramide or ondansetron (if vomiting is refractory to maropitant alone). There are no known additive side effects from using these antiemetics together. ■ **cb**

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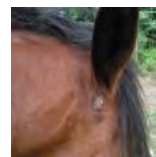
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