Cerenia™
First-in-Class NK-1 Receptor Antagonist Antiemetic for Dogs
Liza le Roux BVSc (Hons) Zoetis, Veterinary Manager - Companion Animal

Cerenia (maropitant citrate) is the first FDA-approved veterinary medication indicated for the prevention and treatment of general emesis and the prevention of vomiting due to motion sickness in dogs. Cerenia is effective and reliable in a broad spectrum of clinical situations involving vomiting due to both central and peripheral stimuli, including vestibular stimuli. Cerenia is non-sedating and with once-daily dosing it is easier for patients and enhances owner compliance. It has a rapid onset of action, within 1 hour of SC administration. The injectable formulation is for clinic use and oral tablets for use both in clinic and at home.

A quick recap: All vomiting stimuli converge in the emetic center! Central and peripheral pathways carry vomiting signals to the emetic center either directly, indirectly, or both.

- The act of vomiting is controlled and coordinated by the vomiting center in the medulla and cannot occur without an intact vomiting center.
- Some vomiting stimuli travel directly to the emetic center, such as those from the higher brain or most gut stimuli. Examples are anxiety, dietary indiscretion and GI motility problems.
- Some vomiting stimuli reach the emetic center indirectly after first being detected by the chemoreceptor trigger zone (CRTZ), examples are chemotherapy, motion sickness (vestibular apparatus) and renal failure.
- Some vomiting stimuli can reach the emetic center both directly and indirectly, for example pancreatitis.

CERENIA targets NK-1 receptors in the emetic center and the CRTZ and inhibits the binding of Substance P.

Substance P is a key neurotransmitter that plays an important part in vomiting - it binds to NK-1 receptors! Vomiting is initiated when Substance P binds to NK-1 receptors in a “lock-and-key” effect.

Maropitant binds to NK-1 receptors and prevents the binding of Substance P, thus preventing vomiting. NK-1 receptors are found in high density in the GI tract, and the brain, including the chemoreceptor trigger zone (CRTZ), the nucleus tractus solitarius (NTS) and the dorsal motor nucleus of the vagus, all collectively referred to as the emetic center. They receive and integrate sensory stimuli from the abdominal viscera, higher cortical areas, and the vestibular system as well as chemical stimuli from the blood and cerebrospinal fluid.

Cerenia is effective in preventing and treating emesis irrespective of whether the stimulus is of central (neural) or peripheral (humoral) origin. Examples of peripherally induced emesis are scavenging gastritis, GI motility problems and primary GI disease. Example of centrally induced emesis is ketoacidosis. Examples of both peripheral and central stimuli are chemotherapy (CRTZ and GI damage), Renal disease +/- uraemia.

Veterinary patient studies

Cerenia has been demonstrated to be significantly more effective to human anti-emetics (metoclopramide) in several veterinary patient studies both in reducing the percentage of dogs that vomit following treatment and the number of vomiting events following treatment.

Metoclopramide is active at both dopaminergic (D2) and serotonergic receptors (5-HT3).

- Metoclopramide is a strong D2 antagonist but a weak 5-HT3 antagonist (peripheral and central)
- To completely block 5-HT3 receptors higher doses of metoclopramide are required.
Therefore metoclopramide does not completely inhibit emesis resulting from peripheral stimulation, and very high doses may be required to do so (with the risk of causing extra-pyramidal effects)\textsuperscript{2,4,5}

Unlike acepromazine, Cerenia is not a sedative and should not be used as a sedative for prevention of vomiting due to motion sickness or any other indication.

Where the frequency of vomiting is high, orally-administered Cerenia tablets may not be absorbed before the next vomiting event occurs and it may be clinically appropriate to use Cerenia solution for injection as initial therapy.

\textbf{Dosing information: Once-daily dosing in 2 convenient formulations.}\n
\textbf{Injectable solution (SC):}\n
For acute canine vomiting—treatment and prevention.

Cerenia can be used to treat or prevent vomiting \textit{either as tablets or as solution for injection} once daily for up to five days.

Cerenia solution for injection should be injected subcutaneously, once daily, at a dose of 1 mg/kg bodyweight (1 ml per 10 kg bodyweight).

The safety of Cerenia solution for injection has not been established in dogs less than 8 weeks of age.

\textbf{Oral tablets:}\n
\textbf{Indications}\n
For use in dogs:

\begin{itemize}
  \item for the prevention of vomiting including that induced by chemotherapy;
  \item for the treatment of vomiting, in conjunction with Cerenia solution for injection and in combination with other supportive measures;
  \item for the prevention of vomiting induced by motion sickness.
\end{itemize}

The safety of Cerenia tablets has not been established in dogs less than 8 weeks of age.

\textbf{For prevention of acute canine vomiting:} Administer orally at 2 mg/kg bodyweight once daily for up to 5 consecutive days.

\textbf{For prevention of motion sickness:} Administer orally at 8 mg/kg bodyweight once daily for up to 2 consecutive days.

Dogs should be dosed 1 hour prior to travel. Tablets may be given with a small amount of food, but do not wrap tightly in food as this may delay absorption and alter efficacy.

\textbf{References:}\n

