

Finally, an FDA-approved drug for canine vomiting...

No, not for stopping it; for initiating it

When it's time to treat canine vomiting, veterinarians have reliable medications in our toolbox. But when it's time to initiate vomiting in an emergency situation, options have been limited and off-label, until now.

By Karen Todd-Jenkins, VMD

Dogs eat things they shouldn't. That's just a fact of life for veterinarians and pet owners. In 2020, the ASPCA Animal Poison Control Center (APCC) handled over 370,000 reports of toxin exposures.¹ The organization recently ranked their most common toxins of 2020, and the top 5 may have a familiar ring. Over-the-counter medications, including NSAIDs, cold remedies, joint rubs, vitamins, and supplements ranked No. 1, representing 17% of the APCC's total case volume. Human prescription medications, such as antidepressants and cardiac medications, ranked No. 2. Human foods, including grapes, raisins, and garlic ranked No. 3, accounting for 13% of the APCC's cases. Chocolate and plants/bouquets round out the top 5. In most of these cases, if ingestion is detected early enough, decontamination usually begins by inducing emesis.

In a survey, veterinarians reported seeing 14 cases per month involving dogs that swallow dangerous items or substances.² So, whether you work in a busy emergency center or a small country practice, you will inevitably need to induce emesis to save a pet's life or prevent severe illness. But our options are relatively limited, aren't they? Apomorphine and 3% hydrogen peroxide are what many veterinarians have available, but these products aren't

FDA-approved for use in dogs, and they have limitations and potential adverse effects that can be concerning. Fortunately, and finally, there's an FDA-approved option specifically for use in dogs.

A NEW SOLUTION

Clevor® (ropinirole ophthalmic solution) is the first FDA-approved emetic for dogs. Clevor is a full dopamine agonist that selectively targets the dopamine D2-type receptors in the brain's chemoreceptor trigger zone (CRTZ). Activation of these receptors transmits information to the brain's vomiting center, which initiates emesis in dogs.³ In cats, the key CRTZ neurotransmitter receptors that initiate vomiting include α 2-adrenergic and 5-HT3 receptors, instead of dopamine. Therefore, Clevor is only approved for use in dogs.

HOW SHOULD CLEVOR BE USED?

Clevor is an ophthalmic solution that's quick and convenient. Clevor's ready-to-use dropper means no mixing, syringes, or complicated dosing calculations are required. Clevor should be applied by dropper into the eye, at a dosage of 1 to 8 drops per dog (divided between both eyes), based on weight. If more than 4 drops are needed (e.g., for large or giant breed dogs), clinicians are advised to wait 2 minutes

before administering the rest of the dose. If emesis doesn't occur within 20 minutes, a second dose may be administered. If required, the second dose will be the exact same number of drops as the first dose.

Each dropper of Clevor is sealed in a single-use aluminum pouch. A single dropper of Clevor provides enough ropinirole to treat a dog weighing from 4 to 220.5 pounds. The dropper and aluminum pouch should be discarded within 30 minutes of opening. However, with a shelf life of 2 years, unopened pouches will remain effective even if your practice doesn't frequently see emergencies that require induction of emesis.

A REVIEW OF CURRENT OPTIONS

Apomorphine and hydrogen peroxide are readily available, but both are used off-label, and neither product is an ideal choice for inducing emesis.

Apomorphine induces emesis by stimulating dopamine receptors in the brain's CRTZ and also has effects on other receptors that are not related to emesis.^{4,5,6} Apomorphine can be administered by intravenous, intramuscular or subcutaneous injection. It also may be administered subconjunctivally, either by direct subconjunctival application of a crushed tablet or diluting a crushed tablet with saline and applying the solution into the

conjunctival sac.⁴ If vomiting doesn't occur, repeated applications are unlikely to induce vomiting.^{4,5,7} Additionally, repeated administration of apomorphine, or high doses of the drug, may actually inhibit vomiting, through its effect on opioid receptors. When apomorphine is applied subconjunctivally, rinsing the eyes with saline solution can suppress further vomiting once the desired result is achieved by removing what has not been absorbed. However, apomorphine can potentially cause protracted vomiting that is not reversible via naloxone, although CNS effects and cardiorespiratory depression, which can also occur, are reversible with naloxone.⁴ Apomorphine must also be purchased through a compounding pharmacy, which can affect product consistency and price.

Hydrogen peroxide (3%) induces vomiting by irritating the oropharynx and stomach lining.⁸ Hydrogen peroxide is readily available and inexpensive. However, it can be messy and difficult to administer, and there is no direct reversal as the way it induces emesis is through irritation of the oropharynx and stomach lining. Potential complications include esophagitis, gastric irritation and ulcers, and duodenal lesions.⁹

Unlike apomorphine and hydrogen peroxide, Clevor is FDA-approved for use in dogs, and scientific studies have demonstrated

its efficacy and safety. In a multi-center, masked, randomized, controlled field study of client-owned dogs of various breeds (ranging in age from 7 months to 15 years), 86% of dogs vomited within 20 minutes following a single application of Clevor. In the same study, 95% of dogs vomited within 30 minutes, and 90% stopped vomiting within 45 minutes.³

Additionally, Clevor's targeted mode of action means that the therapeutic effect can be reversed when desired. Administration of a dopamine receptor antagonist, like metoclopramide (dosage: 0.5 mg/kg intravenously or subcutaneously), can reverse ropinirole's effect and suppress further vomiting.

THE TAKE-HOME MESSAGE

Some pet owners may dismiss dietary indiscretion as harmless "puppy behavior," but the statistics tell a different, more frightening story. Approximately 88% of dogs eat things they shouldn't. And only 23% of these dogs are under 1 year of age.² So clearly these episodes aren't just puppy behavior. Many veterinarians have anecdotes about unusual items they've had to surgically retrieve from a dog's stomach, but these incidents are no laughing matter. As documented by the ASPCA APCC, prescription and over-the-counter medications, inappropriate human foods, and other hazardous items are on the menu for some of our patients. When these emergencies happen, timing is critical. Immediate emesis can be key to improving patient

outcomes, so it's crucial to have a reliable emetic on hand that's safe, effective, and convenient to use.

Clevor is FDA-approved, doesn't require mixing or compounding. In a clinical field study, the mean time to first vomit was 12 minutes, with 3 minutes being the fastest time.³ When necessary, it's also reversible. Before you receive 1 more panicked phone call about a dog that ate chocolate, consider what Clevor can do for your patients and your practice. ■

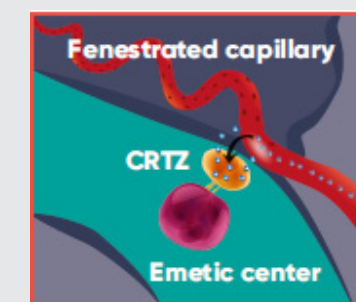
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1. The Official Top 10 Pet Toxins of 2020. ASPCA Animal Poison Control Center. March 25, 2021. Available at: www.aspc.org/news/official-top-10-pet-toxins-2020. Accessed May 5, 2021.
2. Data on file, 2015. Vetoquinol.
3. Clevor® (ropinirole ophthalmic solution) Prescribing Information. Orion Corporation.

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Common side effects after using Clevor may include transient mild or moderate hyperemia of the eye, ocular discharge, protrusion of the 3rd eyelid and blepharospasm, transient mild lethargy, and increased heart rate. All Clevor-related observations resolved within 6 hours post-dosing.³



Clevor (ropinirole) is a full dopamine agonist that selectively targets dopamine D2-type receptors in the brain's chemoreceptor trigger zone (CRTZ), located in the area postrema. Following activation, the CRTZ transmits information to the brain's emetic center to initiate vomiting.

CLEVOR® (ropinirole ophthalmic solution) 30 mg/mL

For ophthalmic use in dogs only
Single use dropper
BRIEF SUMMARY: Before using CLEVOR® (ropinirole ophthalmic solution), please consult the product insert, a summary of which follows:
CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATION: For induction of vomiting in dogs.
DOSE AND ADMINISTRATION: This product should be administered by veterinary personnel.

Dosing Instructions: Administer the appropriate number of eye drops topically according to Table 1. The number of eye drops administered corresponding to body weight results in a target dose of 3.75 mg/m² (dose band 2.7 - 5.4 mg/m²). If the dog does not vomit within 20 minutes of the first dose, then a second dose may be administered.

Dose Administration
4 - 11.1 lbs (1.8 - 5 kgs), 1 drop. Example: 1 drop into either left or right eye. 11.2 - 22.1 lbs (5.1 - 10 kgs), 2 drops. Example: 1 drop into each eye. 22.2 - 44.1 lbs (10.1 - 20 kgs), 3 drops. Example: 2 drops in one eye and 1 drop in the other eye. 44.2 - 77.2 lbs (20.1 - 35 kgs), 4 drops. Example: 2 drops in each eye. 77.3 - 132.3 lbs (35.1 - 60 kgs), 6 drops. Example: an initial dose of 2 drops in each eye, followed 2 minutes later by 1 drop in each eye. 132.4 - 220.5 lbs (60.1 - 100 kgs), 8 drops. Example: an initial dose of 2 drops in each eye, followed 2 minutes later by 2 drops in each eye.

• Wear gloves and protective eye wear when handling or administering this product to prevent accidental exposure.
• Open the dropper by twisting off the tail.

- Keep the dog's head steady in a slightly upright position.
- Hold the dropper in an upright position without touching the eye.
- Rest your finger on the forehead of your dog to maintain the distance between the dropper and the eye.
- Squeeze the prescribed number of drops in to the eye(s).
- CLEVOR is a single use dropper and is light sensitive.
- After administration, with gloves on, return the dropper to the aluminum pouch and place in the carton.
- If the dog does not vomit, a second dose can be given 20 minutes after administration of the first dose.
- This second dose is the same number of drops as the first dose.
- Thirty minutes after opening, with gloves on, dispose of dropper, aluminum pouch, and carton.

Refer to the **Animal Safety Warnings** section for treatment of protracted vomiting.
CONTRAINDICATIONS: Do not use in dogs with central nervous system depression or seizures.
Do not use in cases of ingestion of sharp foreign objects, corrosive agents (acids or alkalis), volatile substances or organic solvents. Do not use in cases with corneal ulceration, ocular irritation, or ocular injury.
Do not use when there is a known sensitivity to ropinirole or the inactive ingredients.

WARNINGS:
Human Safety Warnings: Not for use in humans. Keep out of reach of children.
Wear gloves and protective eye wear when handling or administering this product to prevent accidental exposure. In case of accidental eye, oral or skin exposure, flush with water. If wearing contact lenses, eyes should be rinsed first, then remove contact lenses and continue rinsing. Remove contaminated clothing. Ropinirole is a dopamine agonist. Seek medical attention if accidental

exposure occurs and show the package insert or label to the physician. Exposure to this drug may cause adverse reactions such as headache, nausea, vomiting, dizziness, orthostatic hypotension, and sleepiness. Avoid contact with the product if pregnant, planning to become pregnant, or breast-feeding, as exposure has been shown to have adverse effects on embryo-fetal development based on rodent studies.
Animal Safety Warnings: This product should be administered by veterinary personnel.
Dogs should be monitored for CLEVOR-associated clinical signs, including protracted vomiting, salivation, muscle tremors, evidence of abdominal discomfort, lethargy, transient tachycardia, transient decrease in blood pressure and signs of ocular irritation, including conjunctival hyperemia, mild blepharospasm, and protrusion of the third eyelid. These clinical signs are related to the pharmacological action of ropinirole.
To stop protracted vomiting, administer metoclopramide (dopamine D2 antagonist) at a dose of 0.5 mg/kg intravenously (IV) or subcutaneously (SQ). Metoclopramide also decreases the prevalence of most CLEVOR-associated clinical signs.
PRECAUTIONS: The safe use of CLEVOR has not been evaluated in dogs with cardiac disease or cardiovascular compromise. CLEVOR can cause transient tachycardia and transient decreased systolic blood pressure.
The safe use of CLEVOR has not been evaluated in dogs with hepatic impairment. CLEVOR is metabolized by the liver.
The safe use of CLEVOR has not been evaluated in dogs younger than 4.5 months of age and weight less than 4 pounds.
The safe use of CLEVOR has not been evaluated in dogs that are pregnant, lactating, or intended for breeding.
ADVERSE REACTIONS: Safety was evaluated during a field study that enrolled 132 dogs (100 in the CLEVOR group and 32 in the vehicle control group).

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9. Niedzwecki, A.H., et al. (2017) Effects of oral 3% hydrogen peroxide used as an emetic on the gastroduodenal mucosa of healthy dogs. *J Vet Emerg Crit Care.* 2017; 27(2):178-184.

CLEVOR® is indicated for the induction of vomiting in dogs.

IMPORTANT SAFETY INFORMATION: Do not use in dogs with central nervous system depression or seizures.

Do not use in cases of ingestion of sharp foreign objects, corrosive agents (acids or alkalis), volatile substances or organic solvents. CLEVOR® should not be administered in cases with corneal ulceration, ocular irritation, or ocular injury. Do not use when there is a known sensitivity to ropinirole or the inactive ingredients. **ADVERSE REACTIONS MAY INCLUDE:** Transient mild or moderate hyperemia of the eye, ocular discharge, protrusion of the 3rd eyelid and blepharospasm, transient mild lethargy and increased heart rate. Not recommended for use in breeding, pregnant or lactating dogs. CLEVOR® has not been evaluated in dogs with heart or liver impairments or dogs younger than 4.5 months or less than 4 pounds. Dopamine antagonists, neuroleptics and other medicines with antiemetic properties may reduce the effectiveness of ropinirole. CLEVOR® should be administered by a veterinary professional. Gloves and protective eyewear should be worn when administering. Not for use in humans. Keep out of reach of children.

For complete product safety information, see brief below or visit www.vetoquinolusa.com/clevor-info.

CLEVOR was administered as drops into the eyes at the dose as directed by the dosing table (see **DOSE AND ADMINISTRATION**). The following table shows the number of dogs exhibiting ocular, systemic, and clinical pathology adverse reactions.

Adverse Reactions Reported During the Study (all dogs): Ocular organ system were conjunctival hyperemia, protrusion of the third eyelid, conjunctival discharge, blepharospasm, conjunctival swelling, scratching/rubbing of eyes, corneal ulceration and corneal fluorescein uptake without corneal ulceration. Systemic organ system were lethargy, tachycardia (>160 beats per minute), vomiting duration longer than one hour, salivation, trembling, diarrhea or soft stool, anxious and borborygmi. Clinical pathology organ system were crystalluria, pyuria, increased liver enzymes, decreased blood glucose and increased prothrombin time.

To report suspected adverse events call 1(800) 835-9496, for technical assistance or to obtain a copy of the SDS, contact Vetoquinol USA, Inc. at 1 (800) 267-5707 or www.vetoquinolusa.com.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalad.

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