SUNDAY, 10:00 AM

WHEN MOM UNLEASHES THE VACUUM MONSTER

Safe From Sound

Everyday sounds can trigger real fear in dogs—a serious medical condition called noise aversion. SILEO (dexmedetomidine oromucosal gel) treats noise aversion[1] by helping dogs feel calm.

Stop the noise monsters with resources at **www.sileotools.com**

IMPORTANT SAFETY INFORMATION:

Do not use SILEO in dogs with severe cardiovascular disease, respiratory, liver or kidney diseases, or in conditions of shock, severe debilitation, or stress due to extreme heat, cold or fatigue or in dogs hypersensitive to dexmedetomidine or to any of the excipients. SILEO should not be administered in the presence of preexisting hypotension, hypoxia, or bradycardia. Do not use in dogs sedated from previous dosing. SILEO has not been evaluated in dogs younger than 16 weeks of age or in dogs with dental or gingival disease that could have an effect on the absorption of SILEO. SILEO has not been evaluated for use in breeding, pregnant, or lactating dogs or for aversion behaviors to thunderstorms. Transient pale mucous membranes at the site of application may occur with SILEO use. Other uncommon adverse reactions included emesis, drowsiness or sedation. Handlers should avoid direct exposure of SILEO to their skin, eyes or mouth. Failure to lock the ring-stop on the syringe before dosing SILEO could potentially lead to an accidental overdose. Always review INSTRUCTIONS FOR USE before dispensing and dosing.

See accompanying brief summary of Prescribing Information on page 4.

Reference: 1. SILEO (dexmedetomidine). Prescribing information. Zoetis Inc; 2017.

Sileo®
(dexmedetomidine oromucosal gel)

Noise Aversion: Stop the Suffering with Early Diagnosis and Treatment

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Canine noise aversion—also known as noise anxiety or phobia—affects 67% of dogs in the United States,[1] yet only a small percentage of these dogs are diagnosed and treated. Why are so many dogs not receiving treatment?

The problem is often rooted in how dog owners perceive noise aversion. Many pet owners do not view noise aversion as a medical issue, so they do not discuss their concerns with their veterinarians. Often, pet owners assume that their dog's noise aversion is normal or think they can control their pet's anxiety by holding and comforting them. Unfortunately, both of these assumptions are incorrect. When pet owners are not proactive in discussing their pet's noise aversion, veterinarians miss the opportunity to help address both the problem and their patient.

The causes of noise aversion are not fully understood; however, early exposure to noise may predispose to aversion for some noises and protect from aversion for other noises because of lack of habituation, dishabituation, or sensitization.[2] Genetics has been suggested as a basis for noise aversion for pointers and herding breeds, and the involvement of multiple genes could explain the various presentations.[3,4] Finally, fear is enhanced by repeated exposure to the sound stimulus.[5]

Noise aversion can have a negative effect on the owner's quality of life. Dogs that react to noises occurring in the middle of the night can interrupt their owner's sleep. Owners worry about the wellbeing of dogs that cause property damage and/or self-trauma, and the cost of home repair and veterinary bills may become excessive. This can have a negative effect on the human–animal bond, possibly leading the owner to consider surrender or euthanasia.

BOX 1
Dog Behaviors and Signs During Noise Events

Subtle: Lip licking, yawning, lifting a forelimb

Passive: Freezing, panting, hiding, cowering, trembling

Active: Attention seeking, hypervigilance, pacing, vocalization, inappropriate elimination, trying to escape

DIAGNOSIS

The need to proactively diagnose and treat is overwhelming. First, it is important to understand that dogs experiencing noise aversion are akin to a person having a panic attack. These dogs are suffering, and, therefore, noise aversion is a true welfare concern that should be considered an important medical condition. If left untreated, noise aversion can progress to fear of multiple types of noises, the signs can become more severe, or dogs may require more time to recover after each noise event. Dogs with noise aversion may also develop other comorbidities, such as separation or general anxiety.

The noise aversion checklist (**FIGURE 1**) provides a simple and efficient way to start the discussion about noise aversion. The checklist identifies triggers and signs and helps determine severity. Although thunder and fireworks are the most commonly reported triggers for noise aversion, other everyday noises should also be considered. These can include construction noises (in the house or your neighborhood), garbage trucks, snowplows, doorbells, specific music/tones (phone rings, alarms, sirens), and other street noises. See **TABLE 1** for a complete list of noise triggers.

Many signs can indicate noise aversion (**BOX 1**). Severity can be assessed by asking about the intensity of the reaction, the frequency of noise aversion events, and how soon the dog recovers from the event once the noise has stopped.

TREATMENT

After the diagnosis is made, a multimodal treatment plan can include environmental management, behavior modification, and pharmacologic options. Pharmacologic agents should be initiated early because noise aversion is a neurologic disease and requires medication that can treat the cause.[4] Consultation with a veterinary behaviorist can help in developing a treatment plan.

ENVIRONMENTAL MANAGEMENT

Ideally, the client would prevent exposure to the noise trigger. Because that is not practical in most situations, environmental management can include minimizing the noise by closing the blinds and moving the pet to a soundproof inner room, playing soft music, distracting the dog with a favorite toy or indoor activity, and creating a safe haven. Use of pheromones and wearables may also help the dog feel calmer, but environmental management alone is typically not enough to treat noise aversion.

BEHAVIOR MODIFICATION

Systematic desensitization using commercially available CDs or apps that reproduce the sound of thunder are effective for some dogs with thunderstorm phobia. Counterconditioning techniques can be tailored to the individual patient, and for some patients a combination of these 2 techniques may be required to help manage noise aversion.

PHARMACOLOGIC AGENTS

Although many pharmacologic agents are available, only a few have been show to be effective in published clinical studies, including clonidine,[6] clomipramine,[7,8] trazadone,[9] imepitoin,[10] and dexmedetomidine oromucosal gel.[11] Of these, only the latter two are Food and Drug Administration approved for the treatment of canine noise aversion. Although imepitoin is not expected to be commercially available in the United States until the end of 2020, it comes in 100- and 400-mg tablets. The dosage for noise aversion is 30 mg/kg q 12 h starting 2 days before and continuing through the noise event. In a randomized, placebo-controlled clinical study, 66.2% of the imepitoin-treated dogs had an excellent or good response vs 25% of placebo-treated dogs; the difference was significant at p=0.0001. The most common adverse events included ataxia (34% of treated dogs), increased appetite (18%), and lethargy (11%), rates higher than those in the placebo-treated dogs.[12]

Dexmedetomidine oromucosal gel is an oral agent administered transmucosally and supplied in a 3-mL preloaded syringe. The dose is 125 mcg/m^2; however, with a bioavailability of 28%, only about one fourth of the administered dexmedetomidine is absorbed. At this dose, the agent calms without sedation. It has a flexible dosing schedule and can be administered 30 to 60 minutes before the noise occurs, at the time the noise is first heard, or when the dog begins to show signs. The duration of effect is 2 to 3 hours, so additional doses may be administered if the noise continues or recurs after 2 hours and the dog begins to show signs of noise aversion. Up to 5 doses may be administered for each noise event. In a randomized placebo-controlled clinical study, 75% of the dexmedetomidine-treated dogs had an excellent or good response vs 33% of the placebo-treated dogs (p<0.0001). The most common adverse events included transient pale mucous membranes at the sight of application and emesis (4.4% of the dexmedetomidine-treated dogs). No dogs in the dexmedetomidine group showed excessive signs of sedation.[13]

CONCLUSION

Canine noise aversion is a serious medical condition that requires early diagnosis and treatment to prevent the dog from suffering and improve the dog's quality of life. The noise aversion checklist (**FIGURE 1**) provides a simple and effective way to make the diagnosis. Treatment can be multimodal but should include a pharmacologic option to treat the underlying cause and to provide the best results. ■

References

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TABLE 1 List of Triggers for Noise Aversion

OUTDOOR NOISES	INDOOR NOISES
Fireworks	Doorbells
Thunder	Vacuum cleaners
Outdoor construction	Indoor construction
Sirens and other street noises	Electronic noises (e.g., cell phones, microwaves)
Sporting events at local stadiums	Sporting event on TV
Lawnmowers, other yard tools	Celebrations (family/friends gathering)
Snowplows, garbage trucks	Smoke detectors

SIL-00436

Brief Summary of Prescribing Information

NADA 141-456, Approved by FDA

Sileo®

(dexmedetomidine oromucosal gel)
Each mL of SILEO contains 0.09 mg dexmedetomidine
(equivalent to 0.1 mg dexmedetomidine hydrochloride).
For oromucosal use in dogs only. Not intended for ingestion.

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

INDICATIONS: SILEO is indicated for the treatment of noise aversion in dogs.

CONTRAINDICATIONS:
Do not use SILEO in dogs with severe cardiovascular, respiratory, liver or kidney disease, or in conditions of shock, severe debilitation, or stress due to extreme heat, cold or fatigue. Do not use in dogs with hypersensitivity to dexmedetomidine or to any of the excipients.

WARNINGS:

Human Safety: Not for human use. Keep out of reach of children.

Avoid administering the product if pregnant, as exposure may induce uterine contractions and/or decrease fetal blood pressure.

Appropriate precautions should be taken while handling and using filled syringes. **Impermeable disposable gloves should be worn when handling the syringe, administering SILEO, or when coming in contact with the dog's mouth after application.**

If skin is damaged, dexmedetomidine can be absorbed into the body. In case of skin contact, wash with soap and water. Remove contaminated clothing.

SILEO can be absorbed following direct exposure to skin, eyes, or mouth. In case of accidental eye exposure, flush with water for 15 minutes. If wearing contact lenses, eyes should be rinsed first, then remove contact lenses and continue rinsing, then seek medical advice immediately.

Accidental exposure may cause sedation and changes in blood pressure. In case of accidental exposure, seek medical attention immediately. Exposure to the product may induce a local or systemic allergic reaction in sensitized individuals.

Note to physician: This product contains an alpha-2 adrenoceptor agonist.

The safety data sheet (SDS) contains more detailed occupational safety information. To report adverse reactions in users or to obtain a copy of the SDS for this product call 1-888-963-8471.

Animal Safety: SILEO should not be administered in the presence of pre-existing hypotension, hypoxia, or bradycardia. Sensitive dogs may experience a drop in body temperature and heart rate, and may appear sedated. These dogs should be kept warm and not offered food or water until SILEO's effects have worn off (usually within a few hours). Do not use in dogs sedated from previous dosing.

PRECAUTIONS:
SILEO is not meant to be swallowed. Instead, it must be placed onto the mucosa between the dog's cheek and gum. If SILEO is swallowed, the product may not be effective. If SILEO is swallowed, do not repeat the dose for at least two hours. Feeding and giving treats within 15 minutes after administration should be avoided.

The use of other central nervous system depressants may potentiate the effects of SILEO.

As with all alpha-2 adrenoceptor agonists, the potential for isolated cases of hypersensitivity, including paradoxical response (excitation), exists.

SILEO has not been evaluated in dogs younger than 16 weeks of age or in dogs with dental or gingival diseases that could have an effect on SILEO's absorption. SILEO has not been evaluated for aversion behaviors to thunderstorms.

The safety and effectiveness of SILEO in breeding, pregnant, and lactating dogs has not been evaluated. Administration to pregnant dogs may induce uterine contractions and/or decrease fetal blood pressure.

ADVERSE REACTIONS:
In a well-controlled European field study, which included a total of 182 dogs ranging from 2 to 17 years of age and representing both mixed and pure breed dogs (89 treated with dexmedetomidine oromucosal gel and 93 treated with control), no serious adverse reactions were attributed to administration of dexmedetomidine oromucosal gel.

Table 2 shows the number of dogs displaying adverse reactions (some dogs experienced more than one adverse reaction).

Table 2. Adverse Reactions - Number (%) of dogs

Adverse Reaction	Control N = 93	Dexmedetomidine 125 mcg/m^2 N = 89
Emesis	1 (1.1)	4 (4.5)
Gastroenteritis	0	1 (1.1)
Periorbital edema	0	1 (1.1)
Drowsiness	0	1 (1.1)
Sedation	0	1 (1.1)

Pale mucous membranes were frequently seen in dogs treated with dexmedetomidine oromucosal gel. In most cases, the effect was transient and no adverse reactions due to mucosal irritation were reported.

In a second well-controlled European field study which included a total of 36 dogs ranging from 2 to 17 years of age and representing both mixed and pure breed dogs (12 treated with dexmedetomidine oromucosal gel at 125 mcg/m^2, 12 treated with dexmedetomidine oromucosal gel at 250 mcg/m^2, and 12 treated with a vehicle control), no serious adverse reactions were attributed to administration of dexmedetomidine oromucosal gel. Table 3 shows the number of dogs displaying adverse reactions (some dogs experienced more than one adverse reaction).

Table 3. Adverse Reactions - Number (%) of dogs

Adverse Reaction	Control N = 12	Dexmedetomidine 125 mcg/m^2 N = 12	Dexmedetomidine 250 mcg/m^2 N = 12
Sedation	0	2 (16.7)	4 (33.3)
Lack of effectiveness	4 (33.3)	0	1 (8.3)
Urinary incontinence	0	1 (8.3)	1 (8.3)
Emesis	0	2 (16.7)	0
Head tremor	0	0	1 (8.3)
Inappropriate urination	0	1 (8.3)	0
Ataxia	0	0	1 (8.3)
Mydriasis	0	0	1 (8.3)
Anxiety disorder	0	0	1 (8.3)
Tachypnea	1 (8.3)	0	0
Lethargy	1 (8.3)	0	0
Tachycardia	1 (8.3)	0	0

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS call 1-888-963-8471.

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

HOW SUPPLIED:
SILEO is packaged in HDPE dosing syringe enabling doses from 0.25 to 3 ml. The syringe is fitted with plunger, dosing ring and end cap. Each syringe is further packed into a carton with a label and a leaflet.

Package sizes: (1 syringe per carton) 1 x 3 ml, 3 x 3 ml, 5 x 3 ml, 10 x 3 ml, 20 x 3 ml.

Not all package sizes may be marketed.

STORAGE INFORMATION:

Store unopened and opened syringes in the original package at controlled room temperature 20-25°C (68-77°F) with excursions permitted to 15-30°C (59-86°F). Use syringe contents within 4 weeks after opening the syringe.

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ORION PHARMA
Orion Corporation
Turku, Finland

Dist by:
zoetis
Zoetis Inc.
Kalamazoo, MI 49007

Made in Finland
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FIGURE 1

Does your dog suffer from noise aversion?

Use this checklist to identify triggers and behaviors.

NOISE TRIGGERS

Which of these trigger your dog's behaviorial changes?

- ☐ Fireworks
- ☐ Thunder
- ☐ Celebrations
- ☐ Construction work
- ☐ Traffic or street noise
- ☐ Other

BEHAVIORS

Which behaviors happen during noise events?

- ☐ Pacing
- ☐ Lip licking
- ☐ Trembling or shaking
- ☐ Excessive vigilance or hypervigilance
- ☐ Panting
- ☐ Cowering
- ☐ Hiding
- ☐ Brow furrowed or ears back
- ☐ Freezing or immobility
- ☐ Owner-seeking behavior or abnormal clinginess
- ☐ Refuses to eat
- ☐ Yawning
- ☐ Vocalization (whining or barking at the sounds)

MORE INFORMATION

How often does your dog react to noise triggers?

☐ Once or twice a year ☐ Once or twice a month ☐ Weekly ☐ Daily

Describe the intensity of your dog's reaction to noise triggers:

- ☐ **Mild** – Has a minor impact on our dog's quality of life
- ☐ **Moderate** – Has a modest impact on our dog's quality of life
- ☐ **Severe** – Has a significant impact on our dog's quality of life

How long does it take for your dog to recover from a reaction to noise triggers?

- ☐ **Immediately** after the noise trigger stops
- ☐ **Within an hour** after the noise trigger stops
- ☐ **Several hours** after the noise trigger stops
- ☐ **A day or more** after the noise trigger stops

Download from noise.aversion.checklist.com. This checklist is not a medical diagnostic tool and is not intended to replace discussions with an animal healthcare professional. Discuss medical concerns with your veterinarian.