

PARASITOLOGY

What's New With Parasiticides for Dogs and Cats

*Rachel C. Smith, BS, and Lindsay Starkey, DVM, PhD, DACVM (Parasitology)
Oklahoma State University College of Veterinary Medicine, Stillwater, Oklahoma*

In the past few years, the introduction of isoxazolines and their combination with classic endoparasiticide molecules have drastically changed parasite control and prevention in companion animals. These “end-ectocide” combination preventives provide broad-spectrum parasite coverage in a single monthly product, making them easy for pet owners to administer and thereby often improving compliance.

Several isoxazoline stand-alone and combination preventives for dogs and cats with differing spectra of parasite coverage, application routes, and duration of efficacy are available in the United States; this article provides a quick-reference overview of current label indications.

WHAT'S NEW IN CANINE PARASITICIDES?

In the United States, there are now 3 isoxazoline combination preventives that provide broad-spectrum coverage of both endo- and ectoparasites and 6 isoxazoline stand-alone preventives available for control of ectoparasites in dogs. While the products may appear similar on the surface, each preventive has nuanced label differences and specific highlights (**TABLE 1**).

Over the past 2 years, the isoxazoline combination preventives NexGard PLUS (Boehringer Ingelheim, nexgardforpets.com) and Credelio Quattro (Elanco, elanco.com) have entered the market, and Simparica TRIO (Zoetis, zoetispetcare.com) has undergone

Abstract

Two recent events have drastically changed parasite control and prevention in companion animals: the introduction of isoxazolines and the combined formulation of this class of ectoparasiticides with endoparasiticides. These “end-ectocide” combination preventives are popular with veterinarians and pet owners alike. Broad-spectrum parasite coverage in a single monthly product offers ease of use and peace of mind to pet owners, and these features often lend themselves to improved owner compliance, one of the hardest-fought battles for veterinarians. This article describes some of the newest parasiticides that have come to market for companion animals as well as updated labels for existing preventives, providing a quick-reference resource for general practitioners.



Take-Home Points

- Bravecto Quantum is the newest isoxazoline stand-alone preventive for dogs, the first injectable isoxazoline formulation for dogs, and the only product that provides 12-month flea and tick control in 1 dose.
- Credelio Quattro is the newest isoxazoline-containing monthly preventive for dogs and the only one that incorporates praziquantel and is labeled for treatment of tapeworms.
- Simparica TRIO, NexGard PLUS, and Credelio Quattro have all demonstrated safety when administered in microfilaremic dogs infected with heartworm and in dogs with the *MDR1* (multidrug resistance-1) gene mutation.
- NexGard COMBO is the newest isoxazoline-containing preventive for cats and the only one that incorporates praziquantel and is labeled for treatment of tapeworms.
- Many isoxazoline-containing products are now indicated for control of flea- and tick-transmitted infections through rapidly killing and controlling ectoparasites. The variety of these products means that there are simple parasite preventive options for most pets.

several label updates since its initial FDA approval in 2020. Most recently, Bravecto Quantum (Merck, us.bravecto.com), an injectable isoxazoline preventive, entered the U.S. market in July 2025.

Simparica TRIO

When originally approved, Simparica TRIO was labeled for prevention of heartworm disease caused by *Dirofilaria immitis* and treatment and control of the roundworms *Toxocara canis* and *Toxascaris leonina*, adult hookworms *Ancylostoma caninum* and *Uncinaria stenocephala*, *Ctenocephalides felis* fleas, and 5 tick species: *Amblyomma americanum*, *Amblyomma maculatum*, *Dermacentor variabilis*, *Ixodes scapularis*, and *Rhipicephalus sanguineus*.¹ Treatment and control of *A. caninum* fourth-stage (L4) larvae have since been added to the Simparica TRIO label,² and the invasive Asian long-horned tick, *Haemaphysalis longicornis*, has been added to the labels of both Simparica TRIO and Simparica.^{3,4} *H. longicornis* was introduced to the northeastern region of the United States sometime in the early 2010s but has since been rapidly expanding its distribution south and westward.⁵ Outside of the United States, *H. longicornis* has been implicated in the transmission of a number of tick-borne infections of zoonotic and veterinary importance,⁵ making efficacious control of this species on companion animals a growing concern.

Currently, Simparica TRIO and Simparica are the only isoxazoline-containing preventives to include *A. maculatum*, the Gulf Coast tick, on their labels, and they cover the most tick species of the isoxazoline-containing preventives for dogs. Zoetis has also

emphasized adding vector-borne disease prevention to its parasiticide labels. Both Simparica TRIO and Simparica are now labeled for the prevention of Lyme disease by killing the tick vector *I. scapularis* before transmission of *Borrelia burgdorferi* can occur.^{2,6} In the most recent label extension, Simparica TRIO was shown to be effective for preventing transmission of *Dipylidium caninum*, the flea tapeworm, by killing and controlling *C. felis* fleas.⁷

Simparica TRIO may be prescribed for dogs as young as 8 weeks of age, differing from Simparica, which may only be prescribed for dogs aged 6 months and older.^{1,3} This labeling difference is likely due to the higher minimum dose of sarolaner delivered by Simparica (2 mg/kg) versus Simparica TRIO (1.2 mg/kg).^{1,4}

The safety of macrocyclic lactone-containing preventives is of greater concern in dogs with the multidrug resistance-1 (*MDR1*) gene mutation due to

H. longicornis was introduced to the northeastern region of the United States sometime in the early 2010s but has since been rapidly expanding its distribution south and westward.⁵

their sensitivity to avermectins. Additionally, the use of moxidectin-containing products in dogs that are heartworm positive or have unknown heartworm status often causes concern due to moxidectin's powerful microfilaricidal effect and potential for killing adult heartworms, sometimes called slow-kill. While the use

of moxidectin in heartworm-positive dogs should always be cautioned, Simparica TRIO has demonstrated tolerance and safety in both avermectin-sensitive collies and microfilaremic dogs infected with adult heartworms following administration of up to 3 times the maximum labeled dose.¹

TABLE 1 Isoxazoline-Containing Parasiticides for Dogs

BRAND NAME ^a	FORMULATION	ADMINISTRATION	PARASITES ON LABEL	LABEL HIGHLIGHTS
ISOXAZOLINE COMBINATION PREVENTIVES				
Credelio Quattro (Elanco, elanco.com)	- Lotilaner - Moxidectin - Praziquantel - Pyrantel	- Monthly oral chewable tablet ≥ 8 weeks of age and ≥ 1.5 kg (3.3 lb) - Must be administered with food	- Heartworms - Roundworms - Hookworms - Tapeworms - Fleas - Ticks	Only isoxazoline-containing product for dogs incorporating praziquantel for the treatment of tapeworms
NexGard PLUS (Boehringer Ingelheim, nexgardforpets.com)	- Afoxolaner - Moxidectin - Pyrantel	- Monthly oral chewable tablet ≥ 8 weeks of age and ≥ 1.8 kg (4 lb) - Can be administered with or without food	- Heartworms - Roundworms - Hookworms - Fleas - Ticks	- Improves signs of flea allergy dermatitis as a direct result of eliminating fleas - Efficacious against 3 hookworm species - Prevents transmission of Lyme disease by killing tick vector before transmission
Simparica TRIO (Zoetis, zoetispetcare.com)	- Sarolaner - Moxidectin - Pyrantel	- Monthly oral chewable tablet ≥ 8 weeks of age and ≥ 1.3 kg (2.8 lb) - Can be administered with or without food	- Heartworms - Roundworms - Hookworms - Fleas - Ticks	- Prevents transmission of Lyme disease by killing tick vector before transmission - Prevents transmission of <i>Dipylidium caninum</i> by killing flea vector before transmission
ISOXAZOLINE STAND-ALONE PREVENTIVES				
Bravecto Quantum (Merck, us.bravecto.com)	Fluralaner	- Extended-release injectable suspension ≥ 6 months of age	- Fleas - Ticks	- Only injectable isoxazoline product for dogs - Longest-duration flea and tick control product for dogs
Credelio (Elanco)	Lotilaner	- Monthly oral chewable tablet ≥ 8 weeks of age and ≥ 2 kg (4.4 lb) - Must be administered with food	- Fleas - Ticks	Improves signs of flea allergy dermatitis as a direct result of eliminating fleas
Simparica (Zoetis)	Sarolaner	- Monthly oral chewable tablet ≥ 6 months of age and ≥ 1.3 kg (2.8 lb) - Can be administered with or without food	- Fleas - Ticks	Prevents transmission of Lyme disease by killing tick vector before transmission
Bravecto (topical) (Merck)	Fluralaner	12-week topical solution^b ≥ 6 months of age and ≥ 2 kg (4.4 lb)	- Fleas - Ticks	- Only isoxazoline product for dogs in a topical formulation - Longer-duration flea and tick control product for dogs
Bravecto (chews) (Merck)	Fluralaner	12-week oral chewable tablet^b ≥ 6 months of age and ≥ 2 kg (4.4 lb) - Must be administered with food	- Fleas - Ticks	Longer-duration flea and tick control product for dogs
NexGard (Boehringer Ingelheim)	Afoxolaner	- Monthly oral chewable tablet ≥ 8 weeks of age and ≥ 1.8 kg (4 lb) - Can be administered with or without food	- Fleas - Ticks	- Improves signs of flea allergy dermatitis as a direct result of eliminating fleas - Prevents transmission of Lyme disease by killing tick vector before transmission

^aProducts are arranged in descending order (newest to oldest) by original FDA approval date.

^bEfficacious against *Amblyomma americanum* for 8 weeks only.



NexGard PLUS

When it received FDA approval in 2023, NexGard PLUS was labeled for prevention of heartworm disease caused by *D immitis* and for treatment and control of adult *A caninum*, *Ancylostoma braziliense*, and *U stenocephala*; adult *T canis* and *T leonina*; *C felis* fleas; and 4 tick species: *A americanum*, *D variabilis*, *I scapularis*, and *R sanguineus*.⁸ NexGard PLUS includes 3 different hookworm species on the label, more than any other isoxazoline-containing preventive for dogs. Both NexGard PLUS and NexGard have subsequently added *H longicornis* to their labels, increasing label coverage to 5 tick species.^{9,10} NexGard PLUS and NexGard are also labeled for the improvement of clinical signs associated with flea allergy dermatitis through the killing and elimination of fleas,^{9,10} a unique label claim among isoxazoline-containing preventives for dogs. NexGard PLUS and NexGard are additionally labeled for prevention of *B burgdorferi* infection through the killing of *I scapularis* before transmission can occur.^{11,12} NexGard PLUS and NexGard contain the same minimum dosage of the insecticidal component afoxolaner (2.5 mg/kg).^{9,10}

Both NexGard PLUS and NexGard may be prescribed to dogs as young as 8 weeks, and NexGard PLUS was well tolerated in microfilaremic dogs infected with adult heartworms at up to 3 times the maximum labeled dose and in collies with the *MDR1* gene mutation at up to 5 times the maximum labeled dose.⁸

Credelio Quattro

Credelio Quattro is the newest canine isoxazoline combination preventive to enter the U.S. market, receiving FDA approval in late 2024 and becoming publicly available in 2025.¹³ It is currently the only isoxazoline-containing preventive for dogs to incorporate praziquantel, adding treatment and prevention of 3 tapeworm species to its label: *D caninum*, *Taenia pisiformis*, and *Echinococcus granulosus*.¹³ Credelio Quattro was initially labeled for prevention of heartworm disease caused by *D immitis* and treatment and control of adult *U stenocephala*, *T canis*, and *T leonina*; *C felis* fleas; and 4 tick species: *A americanum*, *D variabilis*, *I scapularis*, and *R sanguineus*.¹³ The label has now been extended to include treatment and control of *A caninum* L4 larvae, immature adults, and adult worms.¹⁴ Compared with moxidectin or pyrantel alone, the combination of the 2 at the labeled doses showed increased efficacy against *A caninum* L4 larvae.¹⁵

With up to 1 year of ectoparasite control, Bravecto Quantum delivers the longest duration of ectoparasite control for dogs in a single injectable dose.

Credelio Quattro may be prescribed for dogs as young as 8 weeks¹³ and has demonstrated tolerance and safety in microfilaremic dogs infected with adult *D immitis* at up to 3 times the labeled dose.¹⁶ Within 1 day of product administration at the labeled dose, experimentally infected dogs showed 38.8% reduction in the number of circulating microfilariae without induction of hypersensitivity reactions.¹⁶

Credelio Quattro has been shown to be safe in collies with the *MDR1* gene mutation and was tolerated at doses up to 5 times the labeled dose while producing only mild dose-dependent adverse effects, which were also observed in normal beagles administered the same dosage.¹⁷ Similarly, NexGard PLUS was well tolerated in dogs with the *MDR1* gene mutation at up to 5 times the maximum labeled dose.⁸ These safety margins differ somewhat from safety studies for Simparica TRIO, in which a dose 5 times the labeled dose produced mild and self-limiting signs, including ataxia and muscle twitching.¹ These differences may be attributable to the lower maximum dose of moxidectin delivered by Credelio Quattro (40 µg/kg) and NexGard PLUS (24 µg/kg) compared with Simparica TRIO (48 µg/kg).^{1,8,13,17}

Bravecto Quantum

Bravecto Quantum is the newest isoxazoline product for dogs to enter the U.S. market. Receiving FDA approval in July 2025, Bravecto Quantum is indicated for treatment and prevention of *C felis* flea infestations and treatment and control of the ticks *I scapularis*, *D variabilis*, and *R sanguineus* for 12 months.¹⁸ Bravecto Quantum is also labeled for treatment and control of *A americanum* for 8 months. With up to 1 year of ectoparasite control, Bravecto Quantum delivers the longest duration of ectoparasite control for dogs in a single injectable dose.

Bravecto Quantum may be prescribed for dogs beginning at 6 months of age and is administered by subcutaneous injection. Nonpainful injection site swelling was the most commonly reported adverse effect in dogs administered Bravecto Quantum; this effect typically resolved over time without intervention.¹⁸ Bravecto Quantum has demonstrated safety when administered at the labeled dosage.

WHAT'S NEW IN FELINE PARASITICIDES?

There are several isoxazoline-containing preventives for cats on the U.S. market, including 3 broad-spectrum isoxazoline combination preventives and 2 isoxazoline stand-alone products (TABLE 2).

Revolution PLUS

In its original 2018 FDA approval, Revolution PLUS (Zoetis, zoetispetcare.com) was labeled for prevention of heartworm disease caused by *D immitis* and for

treatment and control of *Ancylostoma tubaeforme*, *Toxocara cati*, *Otodectes cynotis*, *C felis* fleas, and 3 tick species: *I scapularis*, *A maculatum*, and *D variabilis*.¹⁹ Subsequently, the label was extended to include *A americanum*,²⁰ increasing the labeled coverage to 4 tick species, the highest of any isoxazoline-containing product for cats. Control of *A americanum* is particularly important for cats in the southcentral, southeastern, and mid-Atlantic United States, where this tick serves as the primary vector for transmitting the protozoa *Cytauxzoon felis*, which can cause an estimated 40% or higher mortality rate in cats despite attempted treatment.²¹ In the most recent label extension, Revolution PLUS was shown to be effective for preventing *D caninum* infection in cats by killing and controlling *C felis* fleas.²²

Bravecto PLUS

Initially FDA approved in 2019, Bravecto PLUS (Merck, us.bravecto.com) is labeled for prevention of heartworm disease caused by *D immitis* and treatment

TABLE 2 Isoxazoline-Containing Parasiticides for Cats

BRAND NAME ^a	FORMULATION	ADMINISTRATION	PARASITES ON LABEL	LABEL HIGHLIGHTS
ISOXAZOLINE COMBINATION PREVENTIVES				
NexGard COMBO (Boehringer Ingelheim, nexgardforpets.com)	■ Esafloxolaner ■ Eprinomectin ■ Praziquantel	■ Monthly topical solution ■ ≥ 8 weeks of age and ≥ 0.8 kg (1.8 lb)	■ Heartworms ■ Roundworms ■ Tapeworms ■ Hookworms ■ Fleas ■ Ticks	■ Only isoxazoline-containing product for cats incorporating praziquantel for the treatment of tapeworms ■ Efficacious against 2 hookworm species
Bravecto PLUS (Merck, us.bravecto.com)	■ Fluralaner ■ Moxidectin	■ 2-month topical solution ■ ≥ 6 months of age and ≥ 1.2 kg (2.6 lb)	■ Heartworms ■ Roundworms ■ Hookworms ■ Fleas ■ Ticks	■ Longest-duration isoxazoline-containing product for cats offering both endo- and ectoparasite control
Revolution PLUS (Zoetis, zoetispetcare.com)	■ Selamectin ■ Sarolaner	■ Monthly topical solution ■ ≥ 8 weeks of age and ≥ 1.3 kg (2.8 lb)	■ Heartworms ■ Roundworms ■ Hookworms ■ Ear mites ■ Fleas ■ Ticks	■ Prevents transmission of <i>Dipylidium caninum</i> by killing flea vector before transmission ■ Only isoxazoline-containing product for cats labeled for ear mites
ISOXAZOLINE STAND-ALONE PREVENTIVES				
Credelio CAT (Elanco, elanco.com)	■ Lotilaner	■ Monthly oral chewable tablet ■ ≥ 6 months of age and ≥ 0.9 kg (2 lb) ■ Must be administered with food	■ Fleas ■ Ticks	■ Only isoxazoline product for cats in an oral formulation
Bravecto (topical) (Merck)	■ Fluralaner	■ 12-week topical solution^b ■ ≥ 6 months of age and ≥ 1.2 kg (2.6 lb)	■ Fleas ■ Ticks	■ Longest-duration isoxazoline product for cats

^aProducts are arranged in descending order (newest to oldest) by original FDA approval date.

^bEfficacious against *Dermacentor variabilis* for 8 weeks only.



and control of adults, immature adults, and L4 larvae of *A tubaeformae* and *T cati*; *C felis* fleas; and 2 tick species: *I scapularis* and *D variabilis*.²³ Both the Bravecto PLUS and Bravecto labels have since been extended to include *H longicornis*, making them the only isoxazoline-containing products for cats that are labeled for treatment and control of this invasive tick species.^{24,25}

NexGard COMBO

NexGard COMBO (Boehringer Ingelheim, nexgardforpets.com) is the newest isoxazoline-containing product for cats, receiving initial FDA approval in 2023 for prevention of heartworm disease caused by *D immitis* as well as treatment and control of adults and L4 larvae of *A tubaeformae*, adult *A braziliense*, adult and L4 larvae of *T cati*, *D caninum*, *C felis* fleas, and 2 tick species: *I scapularis* and *A americanum*.²⁶ NexGard COMBO is the only isoxazoline-containing product for cats that contains praziquantel, making it efficacious for treating and controlling *D caninum* tapeworm infections.

NEUROLOGIC CONSIDERATIONS FOR ISOXAZOLINES IN DOGS AND CATS

Many pet owners and veterinarians are conscious of concerns about neurologic adverse events related to isoxazoline use in dogs and cats, particularly following a public FDA alert on the topic in 2023.²⁷ The FDA continues to back the safety of isoxazolines in companion animals but advises that special consideration may be needed for animals with a history of neurologic conditions.²⁷ Animals may have adverse neurologic events with or without a history.

Isoxazolines act against arthropods by binding and inhibiting γ -aminobutyric acid (GABA) and glutamate-gated chloride channels (GluCl_s), resulting in continuous stimulation of the arthropod's neurons, paralysis, and eventual death.²⁸ Mammals also express GABA and GluCl_s; however, limited evidence suggests that isoxazolines have a much higher affinity or specificity for arthropod receptors compared with mammalian receptors.²⁹ Receptor binding differences between the individual isoxazolines, as well as a definitive link between isoxazolines and neurologic effects in mammals, remain undescribed.

Although there are no data on the topic, in animals at elevated risk for adverse neurologic events, veterinarians should consider the potential risk of administering isoxazolines with greater bioavailability or extended duration of activity. While neurologic adverse events are possible, especially in higher-risk animals, isoxazolines appear to be safe in the vast majority of animals that receive these preventives.

SUMMARY

Many parasite preventives for dogs and cats now exist in the U.S. market, and many offer robust control of both endo- and ectoparasites in a single product. Isoxazoline-containing products have grown to dominate the companion animal market due to their robust control of fleas and ticks and the convenient combination of isoxazolines with other molecules that control common intestinal parasites and prevent heartworm disease. With their spectra of parasite coverage and variety in the duration of efficacy, there are preventives to conveniently meet the parasite needs of every dog, cat, and pet owner. **TVP**

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Rachel C. Smith

Rachel Smith is currently a PhD candidate under the mentorship of Dr. Lindsay Starkey at the Oklahoma State University College of Veterinary Medicine (OSU CVM). She earned her BS in animal science from Auburn University in 2020 prior to beginning graduate studies at the Auburn University College of Veterinary Medicine. Her primary research interest is vector-borne infections in companion animals, with a focus on epidemiology and diagnostics. She is also involved as a teaching assistant for parasitology at the OSU CVM and has a strong interest in clinical and diagnostic parasitology. Rachel expects to complete and defend her PhD dissertation in May 2026.



Lindsay Starkey

Dr. Starkey is an associate professor at Oklahoma State University's College of Veterinary Medicine. She earned her BS in animal science from the University of Arkansas and completed her DVM and PhD in veterinary biomedical sciences at Oklahoma State University, where her graduate research focused on several vector-borne infections of dogs. She completed her residency training through the National Center for Veterinary Parasitology at Oklahoma State University. She is involved in various research projects involving vector-borne pathogens, diagnostic parasitology, and parasite consultation and outreach. Dr. Starkey currently serves as a co-director for the National Center for Veterinary Parasitology, editor and board member for the American Heartworm Society, and program chair/president-elect of the American Association of Veterinary Parasitologists.



Disclosures

Dr. Starkey has established professional and paid relationships with Merck, Zoetis, Elanco, and Boehringer Ingelheim.

Ms. Smith has served as a consultant for Zoetis.