

FLEEING FLEAS

Imidacloprid chews, topical solutions, and collars have been shown to treat flea infestations in dogs.



FOCUS ON

Imidacloprid for Removal and Control of Fleas on Dogs

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Imidacloprid is a neonicotinoid insecticide, approved for use in the United States by the Environmental Protection Agency in 1994.¹ It is available as a topical formulation and was approved by the Food and Drug Administration as an oral chewable formulation in 2015.² Imidacloprid is indicated for the treatment of

fleas (adult and larval stages) on dogs and cats; it is often combined with other therapies to treat intestinal parasites, repel ticks, and prevent heartworm infection (**TABLE 1**). Although several options are also available for cats, the focus of this article is imidacloprid efficacy for the control of fleas on dogs.

TABLE 1 Imidacloprid and Imidacloprid Combination Products*

PRODUCT	INGREDIENTS	COVERAGE
SYSTEMIC, ORAL		
Advantus	Imidacloprid 7.5 mg or 37.5 mg	Adult fleas
TOPICAL		
Advantage	Imidacloprid 9.1%	Adult/larval fleas
Advantage II	Imidacloprid 9.1% Pyriproxyfen 0.46%	Adult/larval fleas
K9 Advantix	Imidacloprid 8.8% Permethrin 44%	Adult/larval fleas, ticks, and mosquitoes
K9 Advantix II	Imidacloprid 9.1% Permethrin 44% Pyriproxyfen 0.46%	Adult/larval fleas, ticks, and mosquitoes
Advantage Multi	Imidacloprid 10% Moxidectin 2.5%	Adult/larval fleas Prevention of heartworm, immature hookworm, adult roundworm, and adult whipworm infection
COLLAR		
Seresto	Imidacloprid 10%, Flumethrin 4.5%	Adult/larval fleas, ticks, and mosquitoes

*All products by Bayer (bayer.cvp.service.com and datasheets.scbt.com/sc-361970_mfr.pdf).

EVIDENCE OF EFFICACY

One study involving 32 dogs compared the kill speeds of nitenpyram, selamectin, imidacloprid, and fipronil.³ Each treatment group comprised 8 dogs, and each dog was experimentally infested with 100 fleas. Efficacy at 8 hours after treatment was 100% for nitenpyram, 95.7% for imidacloprid, 74.4% for selamectin, and 46.5% for fipronil.

Another study compared the efficacy of topical fipronil and imidacloprid when used on 23 dogs in flea-infested homes.⁴ Treatments were administered once monthly for 3 months, and flea counts were assessed for the animals and the residences. After treatments, flea counts on the animals were reduced by 99.5% (imidacloprid) and 96.5% (fipronil).

MECHANISM OF ACTION

Imidacloprid acts on the nicotinic acetylcholine receptors at the postsynaptic membranes in the flea, blocking acetylcholine and eventually leading to central nervous system impairment and death. The mechanism of action of imidacloprid is unique, differing from that of other insecticides (e.g., organophosphates, insect growth regulators) in that insect receptors are more sensitive than mammalian receptors to imidacloprid.⁵ This property was originally thought to make imidacloprid more advantageous than other commonly used agricultural insecticides on the market at the time, thereby limiting toxicity and negative effects on other organisms;⁶ however, we now know that this class of insecticides could have significant environmental effects.

PHARMACOKINETICS

When administered orally, imidacloprid is absorbed rapidly and nearly completely from the dog's gastrointestinal tract and reaches effective concentration after about 1.3 hours.⁷ It is distributed throughout the tissues but does not accumulate in the tissues. Its penetration of the blood–brain barrier is poor, which leads to a more favorable safety profile. It is metabolized by the liver to an active metabolite and is eliminated in the urine (70% to 80%) and feces (20% to 30%); terminal half-life is about 2.2 hours.⁵

When applied topically to dogs, imidacloprid is distributed across the skin by translocation and can be found in hair follicles, shed hair, and sebum.⁷ In dogs, systemic absorption of topical preparations seems to be minimal to none.

DOSING AND ADMINISTRATION

For active flea infestations, initial treatment with imidacloprid may be oral or topical. However, its use as monotherapy does not completely prevent infection with other parasites (e.g., heartworms and intestinal parasites).³ Patients should be evaluated to ensure that they are receiving complete parasite prevention regimens with or without imidacloprid augmentation.

When topical formulations of imidacloprid are used, the veterinarian should consult individual product labels to be able to counsel clients on accurate restrictions, such as shampooing and water immersion, before and after application of these products (**TABLE 2**).

TABLE 2 Imidacloprid Product Dosage and Administration*

PRODUCT	DOSAGE AND ADMINISTRATION
SYSTEMIC, ORAL	
Advantus	<ul style="list-style-type: none"> ■ Dosed by weight: 7.5 mg (4–22 lb) or 37.5 mg (23–110 lb). ■ Give 1 soft chew to treat flea infestation. May repeat dose q24h for treatment of flea infestation but should not be used for prevention.
TOPICAL	
Advantage	<ul style="list-style-type: none"> ■ Dosed by weight (see package) every 4 weeks. ■ Apply the entire contents of the tube topically along the dog's back in 3–4 places from shoulder to base of tail.
Advantage II	
K9 Advantix	
K9 Advantix II	
Advantage Multi	
COLLAR	
Seresto	<ul style="list-style-type: none"> ■ Collar sizes: small (≤18 lb) or large (>18 lb). ■ Apply collar and let dog wear continuously for 8 months.

*All products by Bayer (bayer.cvpservice.com and datasheets.scbt.com/sc-361970_mfr.pdf).

ADVERSE EFFECTS, CONTRAINDICATIONS, AND WARNINGS

Adverse Effects

Topical administration of imidacloprid is generally considered to be well tolerated. However, adverse effects may include irritation of the skin at the application site and, in rare cases, pruritus, lethargy, reduced appetite, and hyperactivity.⁵

Oral administration of imidacloprid at labeled doses is also considered to be well tolerated. Reported adverse effects associated with oral administration include vomiting, decreased appetite, lethargy, diarrhea or soft feces, and difficulty walking. Imidacloprid has also been associated with gallbladder mucocele formation, specifically in Shetland sheepdogs.⁸ In 2015, Gookin et al. found that among Shetland sheepdogs, those with gallbladder mucoceles were 9.3 times more likely than controls to have reportedly received imidacloprid.

Contraindications

Use of imidacloprid is contraindicated in puppies younger than 7 weeks of age, dogs weighing less than 3 pounds, and kittens younger than 8 weeks of age. Pertinent clinical considerations should be made before use is recommended in animals that are debilitated, aged, pregnant, nursing, or receiving medication.⁹

Warnings

Clients should be mindful that permethrins can be toxic to cats. Combination products containing permethrins should not be used on cats, and caution should be taken with use of these products on dogs in

households with cats to ensure that the cats are not exposed through grooming or rubbing.

DRUG INTERACTIONS

According to the product label, the oral formulation of imidacloprid may be used concomitantly with other medications (i.e., corticosteroids and antibiotics).^{5,10} Because topically applied imidacloprid is not absorbed systemically, no significant drug–drug interactions have been associated with topical administration of imidacloprid.⁹

In some circumstances, it may be appropriate to treat dogs with more than one product to prevent fleas, ticks, heartworms, and intestinal parasites. Although duplicate therapy to provide full preventive coverage against fleas, ticks, and heartworms should be avoided, some products have been studied in combination and shown to be safe. One such study showed no dermal or systemic safety issues when imidacloprid topical solution was used along with an imidacloprid-containing collar.¹¹ However, in the absence of other studies or evidence, use of products with the same active ingredient or mechanism of action should be avoided.

ENVIRONMENTAL IMPACT

An often-overlooked aspect of parasite prevention is the effect that these insecticides can have on nontarget organisms, ecosystems, and the environment. Neonicotinoids such as imidacloprid can potentially enter the soil and water and negatively affect the environment. A particular concern expressed by the Environmental Protection Agency is that “imidacloprid is classified as very highly toxic to adult honeybees.”¹ An association between agricultural use of neonicotinoid insecticides and honeybee failure and colony collapse has been documented.⁶ Residues have also been found in crop soil and in aquatic ecosystems, affecting their structure and function.⁶ Therefore, to minimize environmental risk when using these products for flea prevention and treatment, care should be taken to follow all directions on product labels.

OFF-LABEL USES

Although imidacloprid is approved and indicated for the removal and control of fleas, it has often been used in an extra-label manner to treat other similar parasitic conditions.

Use of imidacloprid is contraindicated in puppies younger than 7 weeks of age, dogs weighing less than 3 pounds, and kittens younger than 8 weeks of age.

Sarcoptic Mange

In a blinded, randomized controlled efficacy study, 29 dogs with *Sarcoptes scabiei* infestation received either an imidacloprid (10% w/v)/moxidectin (2.5% w/v) combination topically or selamectin topically.¹² Dogs in each group received 2 treatments, 4 weeks apart. After day 22, no *Sarcoptes* mites were found on skin scrapings from any dogs in either treatment group. Clinical signs were nearly entirely resolved by 50 to 64 days after the initial treatment.

Cheyletiellosis

Another study evaluated efficacy of imidacloprid 10%/moxidectin 2.5% topical solution for treating cheyletiellosis (walking dandruff) in dogs.¹³ A total of 20 dogs with microscopy-confirmed cheyletiellosis received 2 treatments with the combination product, 4 weeks apart. On or after day 30 after the first treatment, clinical signs improved but mites were still visible; on or after day 60, no mites or eggs were detected.

Demodicosis

In 2009, a blinded, randomized clinical trial compared efficacy of 2 products for treatment of demodicosis.¹⁴ A total of 50 dogs with demodicosis received either ivermectin daily or imidacloprid 10%/moxidectin 2.5% topical solution applied monthly, every 2 weeks, or weekly. Of the 50 dogs, 35 completed the trial through 4 months or 2 successive examinations with negative skin scrapings. The results showed that the imidacloprid combination product was not significantly more efficacious than ivermectin but that weekly application of imidacloprid was significantly more efficacious than monthly application. Newer agents, however, may prove to be more efficacious in the treatment of demodicosis when given at labeled dosing frequencies. In a recent (2019) study, 16 dogs with naturally acquired demodicosis were randomized to receive 1 treatment of topical fluralaner or 3 treatments of topical imidacloprid/moxidectin at 4-week intervals (or weekly for some with severe cases). Miticidal efficacy of fluralaner was 99.7% at day 28, >99.9% at day 56, and 100% at day 84, whereas efficacy of imidacloprid/moxidectin was 9.8% at day 28, 45.4% at day 56, and 0% at day 84.¹⁵

CLIENT COUNSELING POINTS

- For immediate treatment of flea infestation, give imidacloprid soft chews once daily, as needed, based

on weight. To prevent future infestations, use in conjunction with a preventive product.¹⁰

- Apply topical solutions directly to the skin and allow them to dry thoroughly before the dog comes into contact with other pets or children. Dispose of packaging according to label recommendations.⁹
- Imidacloprid collars provide up to 8 months of protection from fleas and ticks; however, consider replacing collars more frequently for dogs that are frequently immersed in water.⁹
- Because permethrins are toxic to cats, avoid using permethrin-containing combination products in households with cats.
- Although imidacloprid products are generally considered to be well-tolerated, they have the potential to exacerbate gallbladder mucocele formation in Shetland sheepdogs.⁸

SUMMARY

- **Mechanism of action:** Imidacloprid works as an insecticide by acting on nicotinic acetylcholine receptors at the postsynaptic membrane in the flea, blocking acetylcholine and eventually leading to central nervous system impairment and death.
- **Indication:** Imidacloprid may be used for treatment of an active flea infestation; however, it should not be used as monotherapy for flea prevention.³
- **Adverse effects:** Adverse effects of both topical and oral administration are usually mild and transient.
 - Topical administration has been associated with skin irritation at the application site and, more rarely, pruritus, lethargy, reduced appetite, and hyperactivity.
 - Oral administration has been associated with vomiting, decreased appetite, lethargy, and diarrhea/soft stools.
- **Contraindications and warnings:** Use of imidacloprid is contraindicated for puppies younger than 7 weeks, dogs weighing less than 3 pounds, and kittens younger than 8 weeks. Clients should be aware that combination products containing permethrins are toxic for cats.
- **Environmental effects:** The neonicotinoid class of insecticides has been associated with negative effects on nontarget organisms and ecosystems including honeybee colonies, soil of treated crops, and aquatic environments. Veterinarians should be prepared to address clients' concerns about potential negative environmental impacts and the importance of following administration and disposal instructions per packaging. **TVP**

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