

Veterinary Dermatology

Dermatologie vétérinaire

Isoxazolines for treating canine demodicosis, sarcoptic mange (scabies), and lice infestation

Vincent E. Defalque

In 2014, a new class of parasiticides was introduced to the Canadian small animal health market. Isoxazoline drugs include afoxolaner, fluralaner, lotilaner, and sarolaner. A plethora of oral and topical spot-on products are now commercially available and contain either a single isoxazoline or an isoxazoline in combination with 1 or 2 other active ingredient(s). There are geographical differences in the availability and licensure of these drugs. Therefore, one must judiciously consider regional prescribing recommendations. Isoxazolines currently available for use in dogs in Canada are listed in Table 1.

Isoxazolines have had impressive results in controlling canine demodicosis (Figure 1 A, B), sarcoptic mange (scabies) and lice infestation. This article reviews the clinical use (both label and extra label) of isoxazolines in Canada for cutaneous parasites affecting dogs.

Canine demodicosis

Demodicosis is a common skin disease caused by proliferation of *Demodex* mites. The efficacy of isoxazolines was evaluated in 697 dogs enrolled in 20 studies.

Oral afoxolaner

The efficacy of oral afoxolaner was evaluated in 253 dogs enrolled in 7 studies (1–7). Details are summarized in Table 2.

Oral/topical fluralaner

The efficacy of oral or topical fluralaner was evaluated in 373 dogs enrolled in 10 studies (8–17). Details are summarized in Table 3.

Oral lotilaner

The efficacy of oral lotilaner was evaluated in 1 case series (18). Ten dogs were treated orally 3 times, 28 d apart. All dogs were mite-free at Day 70. There were no adverse effects.

Oral sarolaner

The efficacy of oral sarolaner was evaluated in 2 controlled studies. In the first study (19), 8 dogs were treated 3 times, 30 d apart. All dogs were mite-free at Day 44. There were no adverse effects. Another 8 dogs were treated with a weekly spot-on containing imidacloprid and moxidectin. Sarolaner performed better than the spot-on. The second non-inferiority study (20) compared the same 2 products. Fifty-three dogs were treated 30 d apart. All dogs were mite-free at Day 150. Another 28 dogs were treated weekly or monthly with the imidacloprid-moxidectin spot-on. There were no adverse effects with oral sarolaner. Once again, sarolaner performed better than the spot-on.

Dr. Defalque is a Board-certified dermatologist at North West Veterinary Dermatology Services, Vancouver, British Columbia and St. Albert, Alberta.

Address all correspondence to Dr. Vincent Defalque; email: office@vetderm.ca

Use of this article is limited to a single copy for personal study. Anyone interested in obtaining reprints should contact the CVMA office (hbroughton@cvma-acmv.org) for additional copies or permission to use this material elsewhere.

Table 1. Isoxazolines currently available for use in dogs in Canada.

Product name (market year)	Manufacturer	Route	Isoxazoline	Macrocyclic lactone	Other	Label use	Extra-label use
Bravecto (2014)	Merck/Intervet	Oral	Fluralaner	N/A	N/A	F,T	D,S,L
Bravecto topical solution (2018)	Merck/Intervet	Topical	Fluralaner	N/A	N/A	F,T	D,S,L
Bravecto one (2021)	Merck/Intervet	Oral	Fluralaner	N/A	N/A	F,T	D,S,L
Credelio (2019)	Elanco	Oral	Lotilaner	N/A	N/A	F,T	D,S
Credelio plus (2022)	Elanco	Oral	Lotilaner	Milbemycin oxime	N/A	F,T,R,HT	D,S
NexGard (2014)	Boehringer Ingelheim	Oral	Afoxolaner	N/A	N/A	F,T,D	S
NexGard spectra (2019)	Boehringer Ingelheim	Oral	Afoxolaner	Milbemycin oxime	N/A	F,T,D,HK,R,W,HT	S
Simparica (2016)	Zoetis	Oral	Sarolaner	N/A	N/A	F,T	D,S,L
Simparica trio (2020)	Zoetis	Oral	Sarolaner	Moxidectin	Pyrantel	F,T,H,K,R,HT	D,S,L

D — Demodicosis; F — Fleas; HK — Hookworm; HT — Heartworm; L — Lice infestation; R — Roundworm; S — Sarcoptic mange (scabies); T — Ticks; W — Whipworm.
N/A — Not available.



Figure 1. Juvenile demodicosis in a 6-month-old intact male Australian shepherd. Note the facial lesions on initial presentation, including alopecia, erythema, and crusts. Before (Day 0; A) and after (Day 44; B) treatment with a single dose of oral fluralaner.

Canine sarcoptic mange (scabies)

Canine sarcoptic mange (scabies) is a pruritic and contagious skin disease caused by the mite *Sarcoptes scabiei* var. *canis*. The efficacy of isoxazolines was evaluated in 464 dogs enrolled in 9 studies.

Oral afoxolaner

The efficacy of oral afoxolaner was evaluated in 1 controlled study (21). Ten dogs were treated twice, 28 d apart. All dogs were mite-free at Day 28. The efficacy of oral afoxolaner or the combination of afoxolaner-milbemycin oxime was evaluated in 2 case series (22,23). In the first study, 65 dogs were treated twice, 30 d apart; 99.7 to 100% of the dogs were mite-free at Day 60. In the second study, 142 dogs were treated with a single dose. All dogs were mite-free at Day 56. There were no adverse effects in these studies.

Oral/topical fluralaner

The efficacy of oral or topical fluralaner was evaluated in 1 controlled study (24). Nine dogs were treated with a single oral dose and 11 dogs were treated with a single topical spot-on dose. All dogs were mite-free at Day 28. There were no adverse effects. The efficacy of oral fluralaner was evaluated in 1 case series (25).

Seventeen dogs were treated with a single oral dose. All dogs were mite-free at Day 14. Adverse effects were not recorded.

The efficacy of oral or topical fluralaner was evaluated in 1 case series (26). Fifty-four dogs were treated with a single oral dose and 46 dogs were treated with a single topical spot-on dose. All dogs were mite-free at Day 56. There were no adverse effects.

Lastly, the efficacy of a single dose of oral fluralaner was evaluated in 1 case report of crusted — Norwegian-like-scabies (27). The dog was mite-free at Day 30.

Oral lotilaner

The efficacy of oral lotilaner was evaluated in 1 case series (28). Eight dogs were treated orally 3 times, 30 d apart. All dogs were mite-free at Day 30. There were no adverse effects.

Oral sarolaner

The efficacy of oral sarolaner was evaluated in a placebo-controlled laboratory study and in a controlled field study (29). Forty-four dogs were enrolled in the laboratory study. Twenty-two dogs were treated with oral sarolaner, whereas another 22 dogs received a placebo tablet on 2 occasions, 30 d apart. All sarolaner-treated dogs were mite-free at Day 30. Seventy-nine dogs were enrolled in the field study. Fifty-three

Table 2. Canine demodicosis – Afoxolaner studies.

Reference/year	Treatment protocol and outcome
(1) 2016	Controlled study — 8 dogs 3 doses, 14 d apart and a fourth dose 28 d later 100% mite-free at Day 84 No adverse effects Another 8 dogs were treated with a spot-on containing imidacloprid and moxidectin (same intervals) Afoxolaner performed better than the spot-on
(2) 2016	Case series — 4 dogs 3 doses, 28 d apart 100% mite-free at Day 56 Adverse effects not recorded
(3) 2017	Unpublished case series — 102 dogs Treated every 2 to 4 wk 100% mite-free at Day 90 Adverse effects not recorded
(4) 2018	Case series — 6 dogs 1, 2 or 3 doses; 21, 28, 35 or 42 d apart 100% mite-free at Day 77 No adverse effects
(5) 2018	Case series — 15 dogs Treated with the combination of afoxolaner-milbemycin oxime 3 doses, 28 d apart 99.9% mite reduction at Day 84 No adverse effects
(6) 2018	Case series — 50 dogs Treated with afoxolaner (31 dogs) or the combination of afoxolaner-milbemycin oxime (19 dogs) 3 doses, 28 d apart 98% mite reduction at Day 84 Adverse effect: vomiting (1 dog)
(7) 2019	Case series — 68 dogs Treated with the combination of afoxolaner-milbemycin oxime Single dose 82.4% mite reduction at Day 28 Adverse effects not recorded

dogs were treated with oral sarolaner, whereas another 26 dogs were treated with a spot-on containing imidacloprid and moxidectin, twice, 30 d apart. All sarolaner-treated dogs were mite-free at Day 60. Oral sarolaner was noninferior to topically applied imidacloprid/moxidectin. There were no adverse effects in either study.

The efficacy of oral sarolaner was evaluated in 1 case series (26). Twenty-six dogs were treated twice, 28 d apart. All dogs were mite-free at Day 56. There were no adverse effects.

Canine lice infestation

The efficacy of oral fluralaner was evaluated in 1 controlled study (30). Fourteen dogs with a sucking lice infestation caused by *Linognathus setosus* were treated with a single dose. All dogs were lice-free at Day 28. Another 10 dogs were treated once with a spot-on containing permethrin. There were no adverse effects. Fluralaner performed better than the spot-on.

The efficacy of a single oral dose of sarolaner was evaluated in 1 dog with a biting louse infestation caused by *Heterodoxus spiniger* (31). The dog was lice-free at Day 28. There were no adverse effects.

Table 3. Canine demodicosis – Fluralaner studies.

Reference/year	Treatment protocol and outcome
(8) 2015	Controlled study — 8 dogs Single oral dose 100% mite-free at Day 56 No adverse effects Another 8 dogs were treated with a spot-on containing imidacloprid and moxidectin (3 doses, 28 d apart) Oral fluralaner performed better than the spot-on
(9) 2015	Case series — 163 dogs Single oral dose 100% mite-free at Day 60 No adverse effects
(10) 2016	Case series — 4 dogs 2 oral doses, 60 d apart 98% mite reduction at Day 90 Adverse effects not recorded
(11) 2017	Case report — 1 dog with <i>Demodex injai</i> Single oral dose 100% mite-free at Day 49 Adverse effects not recorded
(12) 2018	Case report — 1 dog with hyperadrenocorticism and hypothyroidism Single oral dose 100% mite-free at Day 60 Diffuse nonpruritic erythematous papules on trunk 3 d after administration (resolved spontaneously within a few days)
(13) 2018	Case series — 67 dogs 1 to 3 oral doses, 84 d apart 100% mite-free at Day 90 No adverse effects
(14) 2019	Case series — 20 dogs Single oral dose 100% mite-free at Day 56 No adverse effects
(15) 2019	Controlled study — 8 dogs Single topical spot-on dose 100% mite-free at Day 84 No adverse effects Another 8 dogs were treated with a spot-on containing imidacloprid and moxidectin (at weekly to monthly intervals over 84 d) Topical spot-on fluralaner performed better than the imidacloprid/moxidectin spot-on
(16) 2020	Controlled study — 100 dogs Single oral or topical spot-on dose 100% mite-free at Day 84 (oral) 98% mite-free at Day 84 (topical spot-on) No adverse effects Another 24 dogs were treated with a spot-on containing imidacloprid and moxidectin (at weekly to monthly intervals over 84 d) Oral and topical spot-on fluralaner performed better than the imidacloprid/moxidectin spot-on
(17) 2021	Case report — 1 dog with localized demodicosis Single oral dose 100% mite-free at Day 56

What is the recommend dosage and number of doses?

The number of recommended doses, based on a review of the available scientific literature, is summarized in Table 4. It is recommended to use the labelled dosage for flea and tick

Table 4. Number of recommended doses of isoxazolines (use either a single isoxazoline product or a combination product).

Disease	Number of doses
Canine demodicosis	1 oral or topical dose of fluralaner 3 monthly oral doses of afoxolaner or lotilaner or sarolaner
Canine sarcoptic mange (scabies)	1 oral or topical dose of fluralaner 1 oral dose of afoxolaner 2 monthly oral doses of lotilaner or sarolaner
Canine lice infestation	1 oral or topical dose of fluralaner 1 oral dose of sarolaner

prevention/control/treatment, and to conform to the minimum age and body weight requirements. Due to reduced drug bioavailability in the fasted state, fluralaner and lotilaner should be administered with food, whereas for afoxolaner and sarolaner plasma concentrations are the same, regardless of whether the drug is given with or without food.

What are the potential side effects of isoxazolines?

Isoxazolines have potential side effects (including vomiting, diarrhea, anorexia, lethargy, and seizures). They should only be used in suitable patients (*i.e.*, use with caution in dogs with a history of seizures or neurological disorders), and under veterinary supervision.

Conclusion

The recent introduction of isoxazolines in veterinary medicine has resulted in effective and safe treatment of canine demodicosis, sarcoptic mange (scabies) or lice infestations, with low frequency of administration.

References

1. Beugnet F, Halos L, Larsen D, de Vos C. Efficacy of oral afoxolaner for the treatment of canine generalised demodicosis. *Parasite* 2016;23:14.
2. Chávez F. Case report of afoxolaner treatment for canine demodicosis in four dogs naturally infested with *Demodex canis*. *Int J Appl Res Vet Med* 2016;14:123–127.
3. Mueller RS, Shipstone MA. Update on the diagnosis and treatment of canine demodicosis (workshop report). In: Torres SMF, Roudebush P, eds. *Advances in Veterinary Dermatology*. Vol. 8. Wiley Online Books, 2017:206–207.
4. Iijima Y, Itoh Naoyuki, Kimura Y. Efficacy of afoxolaner in six cases of canine demodicosis. *Jap J Vet Dermatol* 2018;24:83–87.
5. Murayama N, Oshima Y. Efficacy of oral afoxolaner for the treatment of canine generalized demodicosis in Japan. *Vet Dermatol* 2018; 29:269–270.
6. Lebon W, Beccati M, Bourdeau P, *et al.* Efficacy of two formulations of afoxolaner (NexGard and NexGard Spectra) for the treatment of generalised demodicosis in dogs, in veterinary dermatology referral centers in Europe. *Parasit Vect* 2018;11:506.
7. Romero-Núñez C, Guiliana Bautista-Gómez L, Sheinberg G, *et al.* Efficacy of afoxolaner plus milbemycin oxime in the treatment of canine demodicosis. *Intern J Appl Res Vet Med* 2019;17:35–41.
8. Fourie JJ, Liebenberg JE, Horak IG, Taenzler J, Heckerth AR, Frénais R. Efficacy of orally administered fluralaner (Bravecto) or topically applied imidacloprid/moxidectin (Advocate) against generalized demodicosis in dogs. *Parasit Vectors* 2015;8:187.
9. Karas-Tezca J, Dawidowicz J. Efficacy of fluralaner for the treatment of canine demodicosis. *Vet Dermatol* 2015;26:307.

10. Arias PT, Cordero AM. Effectiveness of fluralaner (Bravecto MSD) in treating generalized demodicosis in four dogs. *Vet Dermatol* 2016; 27:112.
11. Benito MM, Sastre N, Ravera I. A case of demodicosis (*Demodex injai*) treated with a novel isoxazoline. *Proc Southern European Veterinary Conf, Granada, Spain, 2017* (abstract).
12. Morita T, Momota Y, Mori A, Oda H, Ike K, Sako T. Successful treatment of refractory demodicosis and transient papules with a single dose of fluralaner in a dog with uncontrolled severe endocrine disease. *J Vet Med Sci* 2018;80:672–675.
13. Duangkaew L, Larsuprom L, Anukkul P, Lekcharoensuk C, Chen C. A field trial in Thailand of the efficacy of oral fluralaner for the treatment of dogs with generalized demodicosis. *Vet Dermatol* 2018;29: 208–e74.
14. Djuric M, Milcic Matic N, Davitkov D, *et al.* Efficacy of oral fluralaner for the treatment of canine generalized demodicosis: A molecular-level confirmation. *Parasit Vectors* 2019;12:270.
15. Fourie JJ, Meyer L, Thomas E. Efficacy of topically administered fluralaner or imidacloprid/moxidectin on dogs with generalised demodicosis. *Parasit Vectors* 2019;12:59.
16. Petersen I, Chiummo R, Zschiesche E, *et al.* A European field assessment of the efficacy of fluralaner (Bravecto) chewable and spot-on formulations for treatment of dogs with generalized demodicosis. *Parasit Vectors* 2020;13:304.
17. Vargo CL, Banovic F. Localized demodicosis in a dog after fluticasone propionate treatment for chronic bronchitis. *Top Companion Anim Med* 2021;45:100578.
18. Snyder DE, Wiseman S, Liebenberg JE. Efficacy of lotilaner (Credelio), a novel oral isoxazoline against naturally occurring mange mite infestations in dogs caused by *Demodex* spp. *Parasit Vectors* 2017;10:532.
19. Six RH, Becskei C, Mazaleski MM, *et al.* Efficacy of sarolaner, a novel oral isoxazoline, against two common mite infestations in dogs: *Demodex* spp. and *Otodectes cynotis*. *Vet Parasitol* 2016;222:62–66.
20. Becskei C, Cuppens O, Mahabir SP. Efficacy and safety of sarolaner against generalized demodicosis in dogs in European countries: A non-inferiority study. *Vet Dermatol* 2018;29:203–e72.
21. Beugnet F, de Vos C, Liebenberg J, Halos L, Larsen D, Fourie J. Efficacy of afoxolaner in a clinical field study in dogs naturally infested with *Sarcoptes scabiei*. *Parasite* 2016;23:26.
22. Hampel V, Knaus M, Schäfer J, Beugnet F, Rehbein S. Treatment of canine sarcoptic mange with afoxolaner (NexGard) and afoxolaner plus milbemycin oxime (NexGard Spectra) chewable tablets: Efficacy under field conditions in Portugal and Germany. *Parasite* 2018;25:63.
23. Romero-Núñez C, Bautista-Gómez LG, Sheinberg G, Martin-Cprdero A, Flores-Ortega A, Heredia-Cárdenas R. Efficacy of afoxolaner plus milbemycin oxime and afoxolaner alone as treatment for sarcoptic mange in naturally infested dogs. *Can J Vet Res* 2020;84:212–216.
24. Taenzler J, Liebenberg J, Roepke RKA, Frénais R, Heckerth AR. Efficacy of fluralaner administered either orally or topically for the treatment of naturally acquired *Sarcoptes scabiei* var. *canis* infestation in dogs. *Parasit Vectors* 2016;9:392.
25. Romero C, Heredia R, Pineda J, *et al.* Efficacy of fluralaner in 17 dogs with sarcoptic mange. *Vet Dermatol* 2016;27:353–e88.
26. Chiummo R, Petersen I, Plehn C, Zschiesche E, Roepke R, Thomas E. Efficacy of orally and topically administered fluralaner (Bravecto) for treatment of client-owned dogs with sarcoptic mange under field conditions. *Parasit Vectors* 2020;13:524.
27. Quilling LL, Lam A, Outerbridge CA, White SD. Treatment of crusted sarcoptic mange with fluralaner in a dog. *Vet Rec* 2021;9:e109.
28. Moog F, Brun J, Bourdeau P, Cadiergues MC. Clinical, parasitological, and serological follow-up of dogs with sarcoptic mange treated orally with lotilaner. *Case Rep Vet Med* 2021;25:6639017.
29. Becskei C, De Bock F, Illambas J, *et al.* Efficacy and safety of a novel oral isoxazoline, sarolaner (Simparica), for the treatment of sarcoptic mange in dogs. *Vet Parasitol* 2016;222:56–61.
30. Kohler-Aanesen H, Saari S, Armstrong R, *et al.* Efficacy of fluralaner (BravectoTM chewable tablets) for the treatment of naturally acquired *Linognathus setosus* infestations on dogs. *Parasit Vectors* 2017;10:426.
31. Barriga RAV, Defalque VE, Rodriguez JG, Morales-Cauti S. Treatment of a biting louse infestation caused by *Heterodoxus spiniger* with sarolaner in one dog. *Jap J Vet Dermatol* 2022;28:11–15.