

# Safety of the concurrent treatment of dogs with topical fluralaner and topical deltamethrin



**Introduction and aim** - Fluralaner is a systemic ectoparasiticide providing flea- and tick-control for twelve weeks following single topical administration. Deltamethrin impregnated collars provide anti-feeding activity against phlebotomine sandfly for 5 months, thereby preventing transmission of *Leishmania ssp.* This study investigated the safety of concurrent topical administration of fluralaner (Bravecto™ spot-on solution for dogs, MSD Animal Health) and deltamethrin (Scalibor™ Protectorband, MSD Animal Health). **Materials and methods** - Ten dogs were fitted one deltamethrin collar for six months and were concurrently administered fluralaner at the maximum clinical dose of 56 mg/kg BW on three occasion (days 0, 56 and 112) topically. The ten dogs in the control group received neither fluralaner nor deltamethrin. All dogs were observed for general health, weighed weekly and examined by a veterinarian at multiple time points throughout the study. Since the study was performed in Australia all dogs received oral moxidectin monthly for heartworm prevention.

**Results and discussion** - Throughout the study period of 24 weeks, there were no clinical findings related to concurrent topical treatment with fluralaner in dogs fitted with a deltamethrin collar. No clinical findings were observed associated with moxidectin administration. Two dogs in the treatment group showed transient localized skin reactions at the collar application site, which were considered to be caused by mechanical irritation and were consistent with the product leaflet. No findings were observed at the topical fluralaner administration site. There were no obvious changes in bodyweights. Concurrent treatment with topical fluralaner is well tolerated in dogs fitted with deltamethrin collar.

Feli Mascha Walther<sup>1\*</sup>,  
Dr.

Petr Fisara<sup>2</sup>,  
BAGSc

Mark Jeremy Allan<sup>3</sup>,  
BVSc

Rainer KA Roepke<sup>4</sup>,  
Dr.

**Keywords** - Bravecto™, Fluralaner, Dog, Safety, Scalibor™, Deltamethrin.

<sup>1</sup> Merck Animal Health 2 Giralda Farms, Madison, NJ, USA.

<sup>2</sup> MSD Animal Health, 26 Artisan Road, Seven Hills, NSW 2172, Australia; petr.fisara@merck.com.

<sup>3</sup> MSD Animal Health Innovation GmbH, Zur Propstei, Schwabenheim 55270, Germany; mark.allan@msd.de.

<sup>4</sup> MSD Animal Health Innovation GmbH, Zur Propstei, Schwabenheim 55270, Germany; rainer.roepke@msd.de

\*Corresponding Author (feli.walther@merck.com)

## INTRODUCTION

**Fluralaner spot-on solution protects dogs from tick and flea infestations and deltamethrin may be used to prevent leishmaniosis.**

Fluralaner (Bravecto™ spot-on solution for dogs, MSD Animal Health) is a systemic ectoparasiticide that provides immediate and persistent insecticidal and acaricidal efficacy in dogs after topical administration<sup>1</sup> and subsequent transdermal absorption<sup>2</sup>. Fluralaner provides at least twelve weeks of flea- and tick-control (*Ctenocephalides felis*, *Ctenocephalides canis*, *Ixodes ricinus*, *Rhipicephalus sanguineus* and *Dermacentor reticulatus*) following topical administration<sup>1</sup>, and fluralaner is also active against mites (*Demodex spp*, *Otodectes cynotis*)<sup>3,4</sup>. Fluralaner was shown to be safe when administered topically at overdoses of up to 5 times the maximum clinical dose at 8-week intervals in healthy Beagle dogs<sup>1</sup>. Deltamethrin (Scalibor™ Protectorband, MSD Animal Health) is available in a collar formulation that provides an anti-feeding effect for 4 to 6 months against ectoparasites including prevention of bites from phlebotomine sandflies for 5 months, the vectors of *Leishmania spp*, and prevention of bites from mosquitos for 6 months<sup>5,6</sup>. Following application of a deltamethrin collar, deltamethrin spreads topically without systemic absorption<sup>5</sup>.

There are no known interactions of fluralaner with other veterinary medicinal drugs<sup>1</sup> like ivermectin<sup>7</sup> or milbemycin oxime plus praziquantel<sup>8</sup>. A previous study investigated the safety of oral fluralaner (Bravecto™ chewable tablets for dogs, MSD Animal Health) when administered concurrently with a topical slow-release formulation of deltamethrin (Scalibor™ Protectorband, MSD Animal Health)<sup>9</sup>: ten dogs were administered fluralaner orally and were also applied a deltamethrin collar, whereas the ten dogs of the control group remained untreated. Since the study was conducted in Australia, all dogs received oral moxidectin for heartworm prevention. Throughout the study period of 24 weeks, there were no clinical findings related to the concurrent treatment with oral fluralaner in dogs fitted with a deltamethrin collar at the recommended dosage regimen. However, this previous investigation did not evaluate the concurrent topical administration of deltamethrin and fluralaner. Therefore, a similar study was conducted to investigate the safety of concurrent use of topical fluralaner with a deltamethrin collar.

## MATERIALS AND METHODS

This study was conducted according to Good Clinical Practices (Good Clinical Practices: International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

(VICH) Guideline 9, 15 June 2000). The study was conducted in Queensland, Australia, after obtaining the authorization of the relevant regulatory authorities (Queensland Department of Agriculture, Fisheries and Forestry; approval no. CA 2014/07/791).

**To investigate the safety of concurrent use, a deltamethrin collar was fitted for six months and fluralaner spot-on solution for dogs was administered three times eight weeks apart.**

20 healthy dogs (14 males and 6 females) of various breeds were included in the study and randomly allocated to two study groups. Animal details are included in Table 1.

Dogs of the treatment group were treated with deltamethrin (Scalibor™ Protectorband collar fitted according to label instructions) and were concurrently administered fluralaner (Bravecto™ spot-on solution) at the maximum clinical dose of 56 mg/kg BW<sup>1</sup> on three occasions, on days 0, 56 and 112 topically between the shoulder blades. Dogs in the control group received neither fluralaner nor deltamethrin, and were treated with paraffin oil (day 0) or saline solution (days 56 and 112) topically between the shoulder blades. All dogs were observed for general health during the first hour following treatment and were examined by a veterinarian at 8, 24, 48, 72 hours, and 7, 14, 21 days after each fluralaner treatment. The veterinarian examined for abnormalities in behaviour, coat and skin including topical solution and collar administration site, locomotion, respiration, eyes, ears, nose, oral cavity, mucous membranes, capillary refill time, pulse palpation, vomitus, feces and urine as present in pen, and any other visible abnormalities. The clinical observations were scheduled to cover the period of highest systemic fluralaner exposure<sup>2</sup> and the time that the deltamethrin collar delivers the maximum expected efficacy following application<sup>5</sup>. Therefore, clinical signs associated with the concurrent use would most likely be apparent at these time points. Veterinary examinations continued on study days 28, 55, 84, 111, 140 and 168 (examinations included assessment for any abnormalities in behaviour, locomotion, auscultation of heart and lung, heart rate, respiratory rate, pulse palpation, mucous membranes, capillary refill time, abdominal palpation, superficial lymph nodes, skin including topical solution and collar administration site, eyes, pupils, ears, nose, mouth, teeth, tongue, anus, vagina, penile orifice, mammary glands, testicles, joints, feet, pads, rectal temperature) and general health observations (observations of dogs in their pen including check of the collar administration site) were performed on all dogs once to twice daily. Body weights were recorded weekly. At monthly in-

**Table 1 - Study group details for evaluation of the safety of topical fluralaner in dogs fitted with a slow release collar formulation of deltamethrin**

Group	Dog ID	Breed	Sex	Age (years)	Body Weight (kg) Day -1	Body Weight (kg) Day 168
<b>Control<sup>a</sup></b>	13	Jack Russell Terrier	Female	0.4	3.6	5.0
	66	Chesapeake Bay Retriever	Male	6.9	32.0	29.9
	92	Chesapeake Bay Retriever	Female	7.9	28.1	27.6
	77	Jack Russell Terrier	Male	6.2	6.3	6.5
	29	Beagle	Male	6.7	10.5	10.2
	52	Labrador Retriever	Male	0.8	23.2	23.3
	11	Jack Russell Terrier	Male	0.4	5.0	6.5
	64	Labrador Retriever	Male	4.5	27.9	26.3
	94	Labrador Retriever	Female	0.8	21.5	21.0
	22	Beagle	Male	0.4	12.4	15.9
	<b>Mean</b>	-	-	<b>3.5</b>	<b>17.0</b>	<b>17.2</b>
	<b>SD</b>	-	-	<b>3.2</b>	<b>10.7</b>	<b>9.6</b>
<b>Treatment<sup>b</sup></b>	46	Labrador Retriever	Female	5.3	21.9	22.9
	81	Chesapeake Bay Retriever	Male	6.7	27.5	29.2
	19	Jack Russell Terrier	Male	0.4	3.9	5.5
	12	Jack Russell Terrier	Male	0.4	4.2	5.7
	18	Jack Russell Terrier	Male	0.4	5.2	6.7
	62	Labrador Retriever	Male	4.5	27.1	25.0
	38	Labrador Retriever	Female	8.3	25.1	24.2
	87	Beagle	Female	1.8	11.1	10.0
	6	Beagle	Male	4.5	15.1	14.2
	4	Jack Russell Terrier	Male	6.2	6.5	6.9
	<b>Mean</b>	-	-	<b>3.9</b>	<b>14.7</b>	<b>15.0</b>
	<b>SD</b>	-	-	<b>2.9</b>	<b>9.9</b>	<b>9.3</b>

<sup>a</sup> Deltamethrin collar applied from day 0 to 168.  
<sup>b</sup> 56 mg fluralaner/kg BW topically on days 0, 56 and 112, deltamethrin collar applied from day 0 to 168.  
 SD: standard deviation.

tervals dogs in both groups also received moxidectin orally at a minimum dose of 3 mcg/kg BW for heartworm prevention<sup>10</sup>, since the study was performed in Australia.

## RESULTS AND DISCUSSION

**Concurrent treatment with topical fluralaner in dogs treated with a slow release collar formulation of deltamethrin is well tolerated.**

Throughout the 24-week study period, there were no clinical findings related to the concurrent treatment with topical fluralaner in dogs fitted with a slow release collar formulation of deltamethrin. No clinical findings were ob-

served in treatment or control group dogs associated with moxidectin administration. All findings were considered incidental and common observations in dog colonies (Table 2), and were not consistent with adverse events specified on the individual product labels<sup>1,5,10</sup>.

Two dogs in the treatment group showed transient localized skin reactions at the collar application site, which were considered to be related to the collar rather than to the concurrent treatment and these observations were consistent with the deltamethrin formulation product leaflet<sup>5</sup>. No findings were observed at the topical fluralaner administration site. Other clinical findings included common health observations in dog colonies like ocular discharge, papilloma or dental tartar; which were not considered to be related to use

**Table 2 - Clinical findings in the treatment and control group**

	Number of dogs affected	
	Treatment group	Control group
<b>Skin lesion at collar administration site*</b>	2	0
<b>Localized skin lesions other than treatment administration site** (macules / flakes / sore / erythema / papules / lesion / scab / papilloma / callus / alopecia)</b>	4	5
<b>Other**</b>	Serous ocular discharge (4), sinus arrhythmia (1), otitis externa (1), dental tartar (2)	Ear mites (1), lameness (1), dental tartar (2), grunting thorax noise (1), serous ocular discharge (1), nasal snuffling sounds (1)

\*Consistent with product label.  
 \*\*None of these observations were considered to be treatment related, because they occurred to a similar incidence in the treatment and control group, were already observed pre-treatment, were transient, were not related to the time of treatment administration, and/or they were only observed in single dogs. All observations were common findings in a dog colony.

of either product alone, or concurrently (Table 2). There were also no obvious or substantial changes in group mean bodyweights during the study (Table 1). Concurrent treatment with topical fluralaner in dogs treated with a slow release collar formulation of deltamethrin is well tolerated. The findings of this study are consistent with previous investigations showing that the con-

current administration of oral fluralaner and topical deltamethrin was well tolerated in dogs.

**ACKNOWLEDGEMENTS**

The authors thank Von Berky Veterinary Services, Kurwongbah, Queensland, Australia, for assistance with the study.

**KEY POINTS**

- Fluralaner spot-on solution protects dogs from tick and flea infestations and deltamethrin may be used to prevent leishmaniosis.
- To investigate the safety of concurrent use, a deltamethrin collar was fitted for six months and fluralaner spot-on solution for dogs was administered three times eight weeks apart.
- There were no clinical findings related to the concurrent administration.
- The concurrent treatment with topical fluralaner in dogs treated with a slow release collar formulation of deltamethrin is well tolerated.

**BIBLIOGRAPHY**

1. European Commission. Product information Bravecto™ spot-on solution for dogs, Annex 1 Summary of product characteristics. In: Community register of veterinary medicinal products. 2017. [http://ec.europa.eu/health/documents/community-register/2016/20160517134628/anx\\_134628\\_en.pdf](http://ec.europa.eu/health/documents/community-register/2016/20160517134628/anx_134628_en.pdf). Accessed April 21, 2017.
2. Kilp S, Ramirez D, Allan MJ *et al*. Comparative pharmacokinetics of fluralaner in dogs and cats following single topical or intravenous administration. *Parasites and Vectors* 9:296-302, 2016.
3. Fourie JJ, Liebenberg JE, Horak IG *et al*. Efficacy of orally administered fluralaner (Bravecto™) or topically applied imidacloprid/moxidectin (Advocate™) against generalized demodicosis in dogs. *Parasites and Vectors* 8:187-193, 2015.
4. Taenzler J, de Vos C, Roepke RKA *et al*. Efficacy of fluralaner against *Otodectes cynotis* infestations in dogs and cats. *Parasites and Vectors* 10:30-35, 2017.
5. SPC\_114758 Scalibor Protectorband 4% w/w 48 cm collar for small and medium sized dogs and SPC\_114757 Scalibor Protectorband 4% w/w 65 cm collar for large sized dogs. 2015. [http://www.vmd.defra.gov.uk/ProductInformationDatabase/SPC\\_Documents/SPC\\_114758.DOC](http://www.vmd.defra.gov.uk/ProductInformationDatabase/SPC_Documents/SPC_114758.DOC). Accessed April 21, 2017.
6. Riassunto delle caratteristiche del prodotto - Scalibor Protectorband 48 cm collare antiparassitario per cani e Riassunto delle caratteristiche del prodotto - Scalibor Protectorband 65 cm collare antiparassitario per cani. 2015. [https://www.vetinfo.sanita.it/j6\\_prontuario/farmacii/public/prodotto/dm/](https://www.vetinfo.sanita.it/j6_prontuario/farmacii/public/prodotto/dm/). Accessed June 01, 2017.
7. Walther FM, Allan MJ, Roepke RKA. Plasma pharmacokinetic profile of fluralaner (Bravecto™) and ivermectin following concurrent administration to dogs. *Parasites and Vectors* 8:508-512, 2015.
8. Walther FM, Fisara P, Allan MJ *et al*. Safety of concurrent treatment of dogs with fluralaner (Bravecto™) and milbemycin oxime - praziquantel. *Parasites and Vectors* 7:481-483, 2014.
9. Walther FM, Fisara P, Allan MJ *et al*. Safety of the concurrent treatment of dogs with Bravecto™ (fluralaner) and Scalibor™ Protectorband (deltamethrin). *Parasites and Vectors* 7:105-106, 2014.
10. U.S. Food and Drug Administration, Center for Veterinary Medicine. NADA 141-051 ProHeart™ for Dogs. 1997. <https://www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/FOIADrugSummaries/ucm116537.htm>. Accessed April 28, 2017.