

A SPECTRUM OF PROTECTION



AGAINST UNSEEN* PARASITES

sentinel
spectrum[®] chews
(milbemycin oxime-lufenuron-praziquantel)

.....

With SENTINEL[®] SPECTRUM[®] Chews, your canine patients and their owners can live life to the fullest—free from fear of parasites they may not see.



*SENTINEL SPECTRUM Chews protects against heartworm disease, 4 intestinal parasites, and prevents flea eggs from hatching.

 **MERCK**
Animal Health

FOR PARASITES THAT GO UNSEEN

PROTECTION
HAPPENS BEHIND
THE SCENES



INVISIBLE BUT NOT INVINCIBLE

They're out there. They're all around us. And even though they may not be seen, they don't have to be a threat to your patients and their owners—not with the comprehensive coverage of SENTINEL SPECTRUM Chews.



Hookworms

Roundworms

Whipworms

Tapeworms

Heartworms

SENTINEL SPECTRUM Chews is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*.^{1,*}

Intestinal parasites

SENTINEL SPECTRUM Chews treats and controls adult hookworm (*Ancylostoma caninum*), adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Dipylidium caninum*, *Echinococcus multilocularis*, *Echinococcus granulosus*, *Taenia pisiformis*) infections.^{1,*}

Immature fleas

SENTINEL SPECTRUM Chews prevents and controls flea populations (*Ctenocephalides felis*). The unique ingredient, lufenuron, prevents flea eggs from hatching.^{1,*}

*Indicated for dogs and puppies two pounds of body weight or greater and six weeks of age and older.

sentinel
spectrum chews
(milbemycin oxime · lufenuron · praziquantel)

COVERAGE YOU CAN TRUST

FOR THE LIFE
THEY SHARE



A SPECTRUM OF CARE FOR THEM

sentinel[®]
spectrum[®] chews
(milbemycin oxime - lufenuron - praziquantel)



DOSING FOR SENTINEL SPECTRUM Chews

Body Weight	Milbemycin Oxime per chew	Lufenuron per chew	Praziquantel per chew	Number of chews
2-8 lbs.	2.3 mg	46 mg	22.8 mg	1
8.1-25 lbs.	5.75 mg	115 mg	57 mg	1
25.1-50 lbs.	11.5 mg	230 mg	114 mg	1
50.1-100 lbs.	23 mg	460 mg	228 mg	1
>100 lbs.	Administer the appropriate combination of chews			

To ensure adequate absorption, always administer SENTINEL SPECTRUM Chews to dogs immediately after or in conjunction with a normal meal.

Shown to be safe

In a margin of safety study, 40 ten-week-old puppies (10 per group) were administered either a placebo or doses of 1, 3, or 5X the maximum exposure dose of SENTINEL SPECTRUM Chews once every 2 weeks for a total of 7 treatments. All clinical signs resolved within 24 hours.¹ SENTINEL SPECTRUM Chews has also been shown to be safe for puppies as young as 6 weeks of age, as demonstrated by a second study.¹

Taste tested

In a field study of 117 dogs, SENTINEL SPECTRUM Chews were found to be especially well-received.¹



sentinel[®]
flavor tabs[®]
(milbemycin oxime + lufenuron)



DOSING FOR SENTINEL FLAVOR TABS

Body Weight	Milbemycin Oxime per tablet	Lufenuron per tablet	Number of tablets
2-10 lbs.	2.3 mg	46 mg	1
11-25 lbs.	5.75 mg	115 mg	1
26-50 lbs.	11.5 mg	230 mg	1
51-100 lbs.	23 mg	460 mg	1

For dogs over 100 lbs, administer the appropriate combination of tablets. To ensure adequate absorption, always administer SENTINEL FLAVOR TABS to dogs immediately after or in conjunction with a normal meal.

You've got options

With SENTINEL[®] FLAVOR TABS[®], you have an alternative that protects against 5 types of parasites. SENTINEL FLAVOR TABS are chewable tablets that do not contain praziquantel, which is used to treat and control adult tapeworms.²

sentinel[®]
spectrum chews
(milbemycin oxime-lufenuron-praziquantel)

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

Description: SENTINEL[®] SPECTRUM[™] Chews are available in four strengths in color-coded packages for oral administration to dogs and puppies according to their weight. Each chewable flavored tablet is formulated to provide a minimum of 0.23 mg/pound (0.5mg/kg) of milbemycin oxime, 4.55 mg/pound (10mg/kg) of lufenuron, and 2.28 mg/pound (5mg/kg) of praziquantel.

Milbemycin oxime consists of the oxime derivatives of 5-dehydrodimilbemycins in the ratio of approximately 80% A₄ (C₂₃H₄₃NO₇, MW 555.71) and 20% A₃ (C₂₃H₄₃NO₇, MW 541.68). Milbemycin oxime is classified as a macrocyclic anthelmintic.

Lufenuron is a benzoylphenylurea derivative with the following chemical composition: N-[2,5-dichloro-4-(1,1,2,3,3,3,3-hexafluoropropoxy)-phenyl-aminocarbonyl]-2,6-difluorobenzamide (C₁₇H₁₂Cl₂F₆N₂O₃, MW 511.15). Benzoylphenylurea compounds, including lufenuron, are classified as insect development inhibitors (IDIs).

Praziquantel is an isoquinolone anthelmintic with the chemical name 2-(Cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4H-pyrazino[2,1-a]isoquinolin-4-one.

Indications: SENTINEL SPECTRUM Chews are indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*, for the prevention and control of flea populations (*Ctenocephalides felis*), and for the treatment and control of adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult hookworm (*Ancylostoma caninum*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Dipylidium caninum*, *Taenia pisiformis*, *Echinococcus multilocularis* and *Echinococcus granulosus*) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

Dosage and Administration: SENTINEL SPECTRUM Chews should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, 4.55 mg/lb (10 mg/kg) lufenuron, and 2.28 mg/lb (5 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes (see **EFFECTIVENESS**).

Dosage Schedule

Body Weight	Milbemycin Oxime per chewable	Lufenuron per chewable	Praziquantel per chewable	Number of chewables
2 to 8 lbs.	2.3 mg	46 mg	22.8 mg	One
8.1 to 25 lbs.	5.75 mg	115 mg	57 mg	One
25.1 to 50 lbs.	11.5 mg	230 mg	114 mg	One
50.1 to 100 lbs.	23.0 mg	460 mg	228 mg	One
Over 100 lbs.	Administer the appropriate combination of chewables			

To ensure adequate absorption, always administer SENTINEL SPECTRUM Chews to dogs immediately after or in conjunction with a normal meal.

SENTINEL SPECTRUM Chews may be offered to the dog by hand or added to a small amount of dog food. The chewables should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole. Care should be taken that the dog consumes the complete dose, and treated animals should be observed a few minutes after administration to ensure that no part of the dose is lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

Heartworm Prevention: SENTINEL SPECTRUM Chews should be administered at monthly intervals beginning within one month of the dog's first seasonal exposure to mosquitoes and continuing until at least 6 months after the dog's last seasonal exposure (see **EFFECTIVENESS**). SENTINEL SPECTRUM Chews may be administered year-round without interruption. When switching from another heartworm preventative product to SENTINEL SPECTRUM Chews, the first dose of SENTINEL SPECTRUM Chews should be given within a month of the last dose of the former product.

Flea Treatment and Prevention: Treatment with SENTINEL SPECTRUM Chews may begin at any time of the year, preferably starting one month before fleas become active and continuing monthly through the end of flea season. In areas where fleas are common year-round, monthly treatment with SENTINEL SPECTRUM Chews should continue the entire year without interruption.

To minimize the likelihood of flea reinfestation, it is important to treat all animals within a household with an approved flea protection product, as necessary.

Intestinal Nematode and Cestode Treatment and Control: Dogs may be exposed to and can become infected with roundworms, whipworms, hookworms, and tapeworms throughout the year, regardless of season or climate. Clients should be advised of appropriate measures to prevent reinfection of their dog with intestinal parasites. Because the prepatent period for *E. multilocularis* may be as short as 26 days, dogs treated at the labeled monthly intervals may become reinfected and shed eggs between treatments.

Contraindications: There are no known contraindications to the use of SENTINEL SPECTRUM Chews.

Warnings: Not for use in humans. Keep this and all drugs out of the reach of children.

Precautions: Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention (see **EFFECTIVENESS**).

Prior to administration of SENTINEL SPECTRUM Chews, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. SENTINEL SPECTRUM Chews are not effective against adult *D. immitis*.

Mild, transient hypersensitivity reactions, such as labored breathing, vomiting, hypersalivation, and lethargy have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Do not use in puppies less than six weeks of age.

Do not use in dogs or puppies less than two pounds of body weight.

The safety of SENTINEL[®] SPECTRUM[™] Chews has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime and lufenuron alone (see **ANIMAL SAFETY**).

Adverse Reactions: The following adverse reactions have been reported in dogs after administration of milbemycin oxime, lufenuron, or praziquantel: vomiting, depression/lethargy, pruritus, urticaria, diarrhea, anorexia, skin congestion, ataxia, convulsions, salivation, and weakness.

To report suspected adverse drug events, contact Merck Animal Health at 1-800-224-5381. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

For technical assistance, call Merck Animal Health at 1-800-224-5318.

Information for Owner or Person Treating Animal: *Echinococcus multilocularis* and *Echinococcus granulosus* are tapeworms found in wild canids and domestic dogs. *E. multilocularis* and *E. granulosus* can infect humans and cause serious disease (alveolar hydatid disease and hydatid disease, respectively). Owners of dogs living in areas where *E. multilocularis* or *E. granulosus* are endemic should be instructed on how to minimize their risk of exposure to these parasites, as well as their dog's risk of exposure. Although SENTINEL SPECTRUM Chews were 100% effective in laboratory studies in dogs against *E. multilocularis* and *E. granulosus*, no studies have been conducted to show that the use of this product will decrease the incidence of alveolar hydatid disease or hydatid disease in humans. Because the prepatent period for *E. multilocularis* may be as short as 26 days, dogs treated at the labeled monthly intervals may become reinfected and shed eggs between treatments.

Effectiveness

Heartworm Prevention: In a well-controlled laboratory study, SENTINEL SPECTRUM Chews (*milbemycin oxime, lufenuron, praziquantel*) were 100% effective against induced heartworm infections when administered once monthly for 6 consecutive months. In well-controlled laboratory studies, neither one dose nor two consecutive doses of SENTINEL SPECTRUM Chews provided 100% effectiveness against induced heartworm infections.

Intestinal Nematodes and Cestodes Treatment and Control: Elimination of the adult stage of hookworm (*Ancylostoma caninum*), roundworm (*Toxocara canis*, *Toxascaris leonina*), whipworm (*Trichuris vulpis*) and tapeworm (*Dipylidium caninum*, *Echinococcus multilocularis*, *Echinococcus granulosus*, *Taenia pisiformis*) infections in dogs was demonstrated in well-controlled laboratory studies.

Flea Prevention and Control: In well-controlled studies, SENTINEL SPECTRUM Chews were effective in preventing flea eggs from hatching, thus providing control of the development of flea populations (*Ctenocephalides felis*).

Palatability: In a field study of 117 dogs offered SENTINEL SPECTRUM Chews, 113 dogs (96.6%) accepted the product when offered from the hand as if a treat, 2 dogs (1.7%) accepted it from the bowl with food, 1 dog (0.9%) accepted it when it was placed in the dog's mouth, and 1 dog (0.9%) refused it.

Animal Safety: In a margin of safety study, 40 ten-week-old puppies (10 per group) were administered either a sham dose (0X) or doses of 1, 3, or 5X the maximum exposure dose of SENTINEL SPECTRUM Chews once every two weeks for a total of seven treatments. Transient ataxia, lethargy, tremors, and salivation were seen in the 3X and 5X groups following each of the seven doses. Lethargy and ataxia were occasionally reported in sham-dosed (0X) and 1X dogs. Tremors were observed twice post-treatment in the 1X treatment group. Vomiting was seen in all treatment groups but at a higher incidence in the 3X and 5X groups. At the 5X dose, shallow breathing was noted in two dogs and one dog was unable to stand following two different doses. All clinical signs resolved within 24 hours.

In a second margin of safety study, 64 six-week-old puppies (16 per group) were dosed with either a sham (0X) or 1, 3, or 5X the maximum exposure dose of SENTINEL SPECTRUM Chews on days 1, 15, 29, and 43. A dose dependent increase in ataxia, decreased activity, tremors, and salivation was seen within 24 hours of treatment. Splayed hind limbs were observed once in one dog in the 5X treatment group. Vomiting was observed in the 5X treatment group.

For SENTINEL SPECTRUM Chews, the maximum exposure based on product dosing is 2.5 mg/kg for milbemycin oxime, 50.7 mg/kg for lufenuron and 25.1 mg/kg for praziquantel, which is higher than the minimum effective dose used in the safety studies for milbemycin oxime and lufenuron (see below).

Milbemycin Oxime: Two studies were conducted in heartworm-infected dogs treated with milbemycin oxime. Mild, transient hypersensitivity reactions were observed in dogs with high microfilariae counts (see **PRECAUTIONS**).

Safety studies in pregnant dogs demonstrated that doses of 0.6X the maximum exposure dose of SENTINEL SPECTRUM Chews, (1.5 mg/kg of milbemycin oxime), administered daily from mating through weaning, resulted in measurable concentrations of milbemycin oxime in milk. Puppies nursing these females demonstrated milbemycin oxime-related effects (depression, decreased activity, diarrhea, dehydration, nasal discharge). A subsequent study, which evaluated the daily administration of 0.6X the maximum exposure dose of SENTINEL SPECTRUM Chews, from mating until one week before weaning, demonstrated no effects on the pregnant females or their litters. A study, in which pregnant females were dosed once, at 0.6X maximum exposure dose of SENTINEL SPECTRUM Chews before, on the day of, or shortly after whelping, resulted in no effects on the puppies.

Some nursing puppies, at 2, 4, and 6 weeks of age, administered oral doses of 9.6 mg/kg milbemycin oxime (3.8X the maximum exposure dose of SENTINEL SPECTRUM Chews) exhibited tremors, vocalization, and ataxia. These effects were all transient and puppies returned to normal within 24 to 48 hours. No effects were observed in puppies administered 0.5 mg/kg milbemycin oxime (minimum label dose).

A rising-dose safety study conducted in rough-coated Collies resulted in ataxia, pyrexia, and periodic recumbency in one of fourteen dogs administered milbemycin oxime at 12.5 mg/kg (5X the maximum exposure dose of SENTINEL SPECTRUM Chews). Prior to receiving the 12.5 mg/kg dose on day 56 of the study, all animals had undergone a dosing regimen consisting of 2.5 mg/kg milbemycin oxime on day 0, followed by 5.0 mg/kg on day 14, and 10.0 mg/kg on day 32. No adverse reactions were observed in any of the Collies treated with doses less than 12.5 mg/kg.

Lufenuron: In a ten-month study, doses of lufenuron up to 2X the maximum exposure dose of SENTINEL SPECTRUM Chews (10 mg/kg) caused no overt toxicity. A single dose of 200 mg/kg had no marked effect on adult dogs, but caused decreased activity and reduced appetite in eight-week-old puppies. Lufenuron tablets were evaluated with concurrent administration of flea adulticides containing carbaryl, permethrin, chlorpyrifos, and cythoate. No toxicity resulted from these combinations. Lufenuron tablets did not cause cholinesterase inhibition nor did they enhance cholinesterase inhibition caused by exposure to organophosphates.

Two laboratory and two well-controlled field studies were conducted to evaluate reproductive safety of lufenuron tablets in breeding dogs. In one of the laboratory studies, in which lufenuron was administered to Beagle dogs as three divided doses, equivalent to 17.8X the maximum exposure dose of SENTINEL SPECTRUM Chews (10 mg/kg), the ratio of gravid females to females mated was 8/8 or 100% in the control group and 6/9 or 67% in the lufenuron-treated group. The mean number of pups per litter was two animals higher in the lufenuron versus control groups and mean birth weights of pups from treated females in this study was lower than control groups. These pups grew at a similar rate to the control pups. The incidence of nasal discharge, pulmonary congestion, diarrhea/dehydration, and sluggishness was higher in the lufenuron-treated pup group than in the control pup group. The incidence of these signs was transient and decreasing by the end of lactation.

Results from three additional reproductive safety studies, one laboratory and two field studies, evaluating eleven breeds of dogs, did not demonstrate any adverse findings for the reproductive parameters measured, including fertility, pup birth weights, and pup clinical signs, after administration of lufenuron up to 1X the maximum exposure dose of SENTINEL SPECTRUM Chews. The average milk blood concentration ratio was approximately 60 (i.e. 60X higher drug concentrations in the milk compared to drug levels in the blood of treated females). Nursing puppies averaged 8-9 times higher blood concentrations of lufenuron compared to their dams.

Storage Information: Store in a dry place at controlled room temperature, between 59° and 77°F (15-25°C).

How Supplied: SENTINEL SPECTRUM Chews are available in four strengths, formulated according to the weight of the dog. Each strength is available in color-coded packages of six chewable tablets each.

Manufactured for: Intervet Inc (d/b/a Merck Animal Health)
2 Giralda Farms
Madison, NJ 07940

Approved by FDA under NADA # 141-333

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The palatable once-a-month prescription tablet that prevents heartworm disease and flea populations in dogs and puppies. SENTINEL[®] FLAVOR TABS[™] (milbemycin oxime/lufenuron) also control flea populations and adult hookworms, and remove and control adult roundworm and whipworm infections in dogs and puppies.

Caution

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

Warnings

Not for human use. Keep this and all drugs out of the reach of children.

Description

SENTINEL FLAVOR TABS are available in four tablet sizes in color-coded packages for oral administration to dogs and puppies according to their weight. (See Dosage Section). Each tablet is formulated to provide a minimum of 0.23 mg/pound (0.5 mg/kg) of milbemycin oxime and 4.55 mg/pound (10 mg/kg) body weight of lufenuron.

Milbemycin oxime consists of the oxime derivatives of 5-dehydrodimilbemycins in the ratio of approximately 80% A₄ (C₂₃H₄₃NO₇, MW 555.71) and 20% A₃ (C₂₃H₄₃NO₇, MW 541.68). Milbemycin oxime is classified as a macrocyclic anthelmintic.

Lufenuron is a benzoylphenylurea derivative with the following chemical composition: N-[2,5-dichloro-4-(1,1,2,3,3,3,3-hexafluoropropoxy)-phenylaminocarbonyl]-2,6-difluorobenzamide (C₁₇H₁₂Cl₂F₆N₂O₃, MW 511.15). Benzoylphenylurea compounds, including lufenuron, are classified as insect development inhibitors (IDIs).

Mode of Action

Milbemycin oxime, one active ingredient in SENTINEL FLAVOR TABS, is a macrocyclic anthelmintic which is believed to act by interfering with invertebrate neurotransmission. Milbemycin oxime eliminates the tissue stage of heartworm larvae and the adult stage of hookworm (*Ancylostoma caninum*), roundworm (*Toxocara canis* and *Toxascaris leonina*) and whipworm (*Trichuris vulpis*) infestations when administered orally according to the recommended dosage schedule.

Lufenuron, the other active ingredient in SENTINEL FLAVOR TABS, is an insect development inhibitor which breaks the flea life cycle by inhibiting egg development. Lufenuron's mode of action is interference with chitin synthesis, polymerization and deposition. Lufenuron has no effect on the adult flea. After biting a lufenuron-treated dog, the female flea ingests a blood meal containing lufenuron which is subsequently deposited in her eggs. Lufenuron prevents most flea eggs from hatching or maturing into adults and thus prevents and controls flea populations by breaking the life cycle. (See Efficacy).

Indications

SENTINEL FLAVOR TABS are indicated for use in dogs and puppies, four weeks of age and older, and two pounds body weight or greater. SENTINEL FLAVOR TABS are also indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*, for the prevention and control of flea populations, the control of adult *Ancylostoma caninum* (hookworm), and the removal and control of adult *Toxocara canis* and *Toxascaris leonina* (roundworm) and *Trichuris vulpis* (whipworm) infections.

Lufenuron controls flea populations by preventing the development of flea eggs and does not kill adult fleas. Concurrent use of an adulticide product may be necessary for adequate control of adult fleas.

Without concurrent use of an adulticide, adequate flea control may not be achieved in dogs that have repeated exposure to flea infested animals or environments.

Precautions

Do not use in puppies less than four weeks of age and less than two pounds of body weight. Prior to administration of SENTINEL FLAVOR TABS, dogs should be tested for existing heartworm infections. Infected dogs should be treated to remove adult heartworms and microfilariae prior to initiating treatment with SENTINEL FLAVOR TABS. Mild, transient hypersensitivity reactions manifested as labored respiration, vomiting, salivation and lethargy have been noted in some treated dogs carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

SENTINEL FLAVOR TABS immediately break the flea life cycle by inhibiting egg development. However, preexisting flea populations may continue to develop and emerge after treatment with SENTINEL FLAVOR TABS has begun. Based on results of clinical studies, this emergence generally occurs during the first 30-60 days. Therefore, noticeable control may not be observed until several weeks after dosing when a preexisting infestation is present. Cooler geographic areas may have longer lag periods due to a prolonged flea life cycle. The concurrent use of an approved adulticide may be employed depending on the severity of the infestation.

If a SENTINEL FLAVOR TABS-treated dog comes in contact with a flea-infested environment, adult fleas may infest the treated animal. These adult fleas are unable to produce viable offspring. The temporary use of an adulticide product may be necessary to kill these adult fleas.

Efficacy: Milbemycin Oxime

Milbemycin oxime provided complete protection against heartworm infection in both controlled laboratory and clinical trials.

In laboratory studies, a single dose of milbemycin oxime at 0.5 mg/kg was effective in removing roundworms, hookworms and whipworms. In well-controlled clinical trials, milbemycin oxime was also effective in removing roundworms and whipworms and in controlling hookworms.

Efficacy: Lufenuron

Lufenuron provided 99% control of flea egg development for 32 days following a single dose of lufenuron at 10 mg/kg in studies using experimental flea infestations. In well-controlled clinical trials, when treatment with lufenuron tablets was initiated prior to the flea season, mean flea counts were lower on lufenuron-treated dogs versus placebo-treated dogs. After 6 monthly treatments, the mean number of fleas on lufenuron-treated dogs was approximately 4 compared to 230 on placebo-treated dogs.

When treatment was initiated during the flea season, lufenuron tablets were effective in controlling flea infestations on dogs that completed the study. The mean flea count per lufenuron-treated dog was approximately 74 prior to treatment but had decreased to 4 after six monthly doses of lufenuron. A topical adulticide was used in the first eight weeks of the study to kill the pre-existing adult fleas.

Safety: Milbemycin Oxime

Milbemycin oxime has been tested safely in over 75 different breeds of dogs, including collies, pregnant females, breeding males and females, and puppies over two weeks of age. In well-controlled clinical field studies 786 dogs completed treatment with milbemycin oxime. Milbemycin oxime was used safely in animals receiving frequently used veterinary products such as vaccines, anthelmintics, antibiotics, steroids, flea collars, shampoos and dips.

Two studies in heartworm-infected dogs were conducted which demonstrated mild, transient hypersensitivity reactions in treated dogs with high microfilaremia counts (see Precautions for reactions observed). Safety studies in pregnant dogs demonstrated that high doses (1.5 mg/kg – 3X) of milbemycin oxime given in an exaggerated dosing regimen (daily from mating through weaning), resulted in measurable concentrations of the drug in milk. Puppies nursing these females which received exaggerated dosing regimens demonstrated milbemycin-related effects. These effects were directly attributable to the exaggerated experimental dosing regimen. The product is normally intended for once-a-month administration only. Subsequent studies included using 3X daily from mating to one week before weaning and demonstrated no effects on the pregnant females or their litters. A second study where pregnant females were dosed once at 3X the monthly use rate either before, on the day of or shortly after whelping resulted in no effects on the puppies.

Some nursing puppies, at 2, 4, and 6 weeks of age, given greatly exaggerated oral doses of milbemycin oxime (9.6 mg/kg = 19X) exhibited signs typified by tremors, vocalization and ataxia. These effects were all transient and puppies returned to normal within 24 to 48 hours. No effects were observed in puppies given the recommended dose of milbemycin oxime (0.5 mg/kg). This product has not been tested in dogs less than 2.2 pounds in body weight.

A rising-dose safety study conducted in rough-coated collies manifested a clinical reaction consisting of ataxia, pyrexia and periodic recumbency in one of fourteen dogs treated with milbemycin oxime at 12.5 mg/kg (25X monthly use rate). Prior to receiving the 12.5 mg/kg dose (25X monthly use rate) on day 56 of the study, all animals had undergone an exaggerated dosing regimen consisting of 2.5 mg/kg milbemycin oxime (5X monthly use rate) on day 0, followed by 5.0 mg/kg (10X monthly use rate) on day 14 and 10.0 mg/kg (20X monthly use rate) on day 32. No adverse reactions were observed in any of the collies treated with this regimen up through the 10.0 mg/kg (20X monthly use rate) dose.

Safety: Lufenuron

Lufenuron tablets have been used and tested safely in over forty breeds of dogs, including pregnant females, breeding males and puppies over six weeks of age. In well-controlled clinical trials, 151 dogs completed treatment with lufenuron tablets. Lufenuron tablets were used safely in animals receiving frequently used veterinary products such as vaccines, anthelmintics, antibiotics and steroids. In a ten-month study, doses up to 10X the recommended dose rate of 10 mg/kg caused no overt toxicity. A single dose of 200 mg/kg (20X the recommended dose rate) had no marked effect on adult dogs, but caused decreased activity and appetite in eight week old puppies. Mean body weights of male and female puppies were higher in treated versus control group at the end of the study. In specifically designed target animal safety studies, lufenuron tablets were tested with concurrent administration of flea adulticides containing carbaryl, permethrin, chlorpyrifos and cythoate. No toxicity resulted from these combinations. Lufenuron tablets did not cause cholinesterase inhibition nor did they enhance cholinesterase inhibition caused by exposure to organophosphates.

Four reproductive safety studies were conducted in breeding dogs with lufenuron tablets: two laboratory and two well-controlled clinical studies. In one of the laboratory studies, where lufenuron was administered to beagle dogs at doses equivalent to 90X (3X daily) the monthly recommended dose of 10 mg/kg, the ratio of gravid females to females mated was 8/8 or 100% in the control group and 6/9 or 67% in the lufenuron-treated group. The mean number of pups per litter was two animals higher in the treated versus control groups and the mean birth weights of pups from treated females in this study was lower than control groups.

These pups grew at a similar rate to control pups. There was a higher incidence of four clinical signs in the lufenuron-treated versus control group: nasal discharge, pulmonary congestion, diarrhea/dehydration and sluggishness. The incidence of these signs was transient and decreasing by the end of lactation. Results from three additional reproductive safety studies, one laboratory and two clinical field studies evaluating eleven breeds of dogs, did not demonstrate any adverse findings for the reproductive parameters measured including fertility, pup birth weights and pup clinical signs after administration of lufenuron up to 5X the recommended monthly use rate.

Data from analysis of milk from lactating animals treated with lufenuron tablets at 2X and 6X the recommended monthly use rate demonstrates that lufenuron concentrates in the milk of these dogs. The average milk/blood concentration ratio was approximately 60 (i.e., 60X higher drug concentrations in the milk compared to drug levels in the blood of treated females). Nursing puppies averaged 8-9 times higher blood concentrations of lufenuron compared to their dams.

Dosage

SENTINEL FLAVOR TABS are given orally, once a month, at the recommended minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime and 4.55 mg/lb (10mg/kg) lufenuron. Dogs over 100 lbs are provided the appropriate combination of tablets.

Administration

<p>TO ENSURE ADEQUATE ABSORPTION, ALWAYS ADMINISTER SENTINEL FLAVOR TABS TO DOGS IMMEDIATELY AFTER OR IN CONJUNCTION WITH A NORMAL MEAL.</p>

SENTINEL FLAVOR TABS are palatable and most dogs will consume the tablet when offered by the owner. As an alternative to direct dosing, the tablets can be hidden in food. Be certain the dog consumes the entire tablet or tablets.

Administer SENTINEL FLAVOR TABS to dogs immediately after or in conjunction with a normal meal. Food is essential for adequate absorption of lufenuron. Watch the dog closely following administration to be sure the entire dose has been consumed. If it is not entirely consumed, redose with the full recommended dose as soon as possible.

SENTINEL FLAVOR TABS must be administered monthly, preferably on the same date each month. Treatment with SENTINEL FLAVOR TABS may begin at any time of year. In geographic areas where mosquitoes and fleas are seasonal, the treatment schedule should begin one month prior to the expected onset and should continue until the end of "mosquito and flea season." In areas with year-round infestations, treatment should continue through the entire year without interruption.

If a dose is missed and a 30-day interval between dosing is exceeded, administer SENTINEL FLAVOR TABS immediately and resume the monthly dosing schedule. If SENTINEL FLAVOR TABS replace daily diethylcarbamazine (DEC) for heartworm prevention, the first dose must be given within 30 days after the last dose of DEC.

Adverse Reactions

The following adverse reactions have been reported in dogs after giving milbemycin oxime or lufenuron: vomiting, depression/lethargy, pruritus, urticaria, diarrhea, anorexia, skin congestion, ataxia, convulsions, hypersalivation, and weakness.

To report suspected adverse drug events, contact Merck Animal Health at 1-800-224-5318. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

How Supplied

SENTINEL FLAVOR TABS are available in four tablet sizes (see Dosage section) formulated according to the weight of the dog. Each tablet size is available in color-coded packages of 6 or 12 tablets each, which are packaged 10 per display carton.

Storage Conditions

Store in a dry place at controlled room temperature, between 59° and 77°F (15-25°C).

Questions? Comments?
Please Call 1-800-224-5318
Visit our website at SentinelPet.com

Manufactured for:
Intervet Inc (d/b/a Merck Animal Health)
2 Giralda Farms
Madison, NJ 07940

Approved by FDA under NADA # 141-084

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PRESCRIBE A SPECTRUM OF PROTECTION



Heartworms



Hookworms*



Roundworms



Whipworms



Tapeworms



Immature Fleas†

To order SENTINEL SPECTRUM Chews for your clinic, please contact your Merck Animal Health sales representative.

sentinel
spectrum® chews
(milbemycin oxime - lufenuron - praziquantel)



sentinel^{flavor}
tabs®
(milbemycin oxime - lufenuron)

IMPORTANT SAFETY INFORMATION:

SENTINEL® SPECTRUM® Chews (milbemycin oxime/lufenuron/praziquantel). Dogs should be tested for heartworm prior to use. Mild hypersensitivity reactions have been noted in some dogs carrying a high number of circulating microfilariae. Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. See inside for full product information.

SENTINEL® FLAVOR TABS® (milbemycin oxime/lufenuron). Dogs should be tested for heartworm prior to use. In a small percentage of treated dogs, digestive, neurologic, and skin side effects may occur. See inside for full product information.

**A. caninum*.

†Prevents flea eggs from hatching.

Reference: 1. SENTINEL® SPECTRUM® Chews [product label]. Madison, NJ: Intervet, Inc.; 2020. 2. SENTINEL® FLAVOR TABS® [product label]. Madison, NJ: Intervet, Inc.; 2020.

