

INTERCEPTOR™ PLUS (milbemycin oxime/praziquantel)

Caution

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

Description

INTERCEPTOR PLUS is 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 (0.5 mg/kg) of milbemycin oxime and 2.28 mg/pound (5 mg/kg) of praziquantel.

Milbemycin oxime consists of the oxime derivatives of 5-didehydromilbemycins in the ratio of approximately 80% A₄ (C₃₂H₄₅NO₇, MW 555.71) and 20% A₃ (C₃₁H₄₃NO₇, MW 541.68). Milbemycin oxime is classified as a macrocyclic anthelmintic.

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

INTERCEPTOR PLUS is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*; and for the treatment and control of adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult hookworm (*Ancylostoma caninum*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Taenia pisiformis*, *Echinococcus multilocularis*, *Echinococcus granulosus*, and *Dipylidium caninum*) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

Dosage and Administration

INTERCEPTOR PLUS should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, 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	Praziquantel per chewable	Number of chewables
2 to 8 lbs.	2.3 mg	22.8 mg	One
8.1 to 25 lbs.	5.75 mg	57 mg	One
25.1 to 50 lbs.	11.5 mg	114 mg	One
50.1 to 100 lbs.	23 mg	228 mg	One
Over 100 lbs.	Administer the appropriate combination of chewables.		

INTERCEPTOR PLUS 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 for 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:

INTERCEPTOR PLUS should be administered at monthly intervals beginning within 1 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**). INTERCEPTOR PLUS may be administered year-round without interruption. When switching from another heartworm preventative product to INTERCEPTOR PLUS, the first dose of INTERCEPTOR PLUS should be given within a month of the last dose of the former product.

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 INTERCEPTOR PLUS.

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 INTERCEPTOR PLUS, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. INTERCEPTOR PLUS is 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 INTERCEPTOR PLUS has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime alone (see **ANIMAL SAFETY**).

Adverse Reactions

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

To report suspected adverse drug events, contact Elanco US Inc. at 1-888-545-5973 or the FDA at 1-888-FDA-VETS.

For technical assistance call Elanco US Inc. at 1-888-545-5973.

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 INTERCEPTOR PLUS was 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, INTERCEPTOR PLUS was 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 INTERCEPTOR PLUS 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 (*Echinococcus multilocularis*, *Echinococcus granulosus*, *Taenia pisiformis* and *Dipylidium caninum*) infections in dogs was demonstrated in well-controlled laboratory studies.

Palatability

In a field study of 115 dogs offered INTERCEPTOR PLUS, 108 dogs (94.0%) accepted the product when offered from the hand as if a treat, 1 dog (0.9%) accepted it from the bowl with food, 2 dogs (1.7%) accepted it when it was placed in the dog's mouth, and 4 dogs (3.5%) refused it.

Animal Safety

INTERCEPTOR PLUS:

In a repeated dose safety study, 40 ten-week-old puppies (10 per group) were dosed with either a sham dose (0X) or 1, 3, or 5X the maximum label exposure of INTERCEPTOR PLUS every 14 days for a total of seven treatments. Ataxia, lethargy, and salivation were seen in the 3X and 5X treated dogs following each of the seven doses. Vomiting was seen in all treatment groups but had a higher incidence in the 3X and 5X treatment groups.

In a repeated dose safety study, 64 six-week-old puppies (16 per group) were dosed with either a sham dose (0X) or 1, 3, or 5X the maximum label exposure of INTERCEPTOR PLUS every 14 days for a total of four treatments. Lethargy was observed in all groups. Ataxia was observed in the three treated groups, including one dog in the 1X treated group. For both lethargy and ataxia the incidence and duration increased in the 3X and 5X groups. These signs were observed during the first 24 hours following treatment. Salivation and tremors were observed in the 3X and 5X treated dogs beginning immediately after dosing and up to six hours post dose. Vomiting was only observed in the 5X treatment group on most, but not all, treatment days.

For INTERCEPTOR PLUS the maximum exposure based on product dosing is 2.5 mg/kg for milbemycin oxime and 25.1 mg/kg for praziquantel, which is higher than the minimum effective dose used in the safety studies for milbemycin oxime (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 INTERCEPTOR PLUS, (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 INTERCEPTOR PLUS, 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 the maximum exposure dose of INTERCEPTOR PLUS 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 INTERCEPTOR PLUS) 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 INTERCEPTOR PLUS). 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.

Storage Information

Store at room temperature, between 59° and 77°F (15-25°C).

How Supplied

INTERCEPTOR PLUS is 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. The tablets containing 2.3 mg milbemycin oxime/22.8 mg praziquantel or 5.75 mg milbemycin oxime/57 mg praziquantel are also available in color coded packages of one chewable tablet each.

Manufactured for:

Elanco US Inc.
Greenfield, IN 46140, USA
Product of Japan

NADA #141-338, Approved by FDA

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