

COMFORTIS- spinosad tablet, chewable
Elanco US Inc.

Comfortis™
(spinosad)

Chewable Tablets

COMFORTIS™ -Cats

(spinosad)

Chewable Tablets

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

Description:

COMFORTIS (spinosad) is available in three sizes of chewable flavored tablets for oral administration to cats and kittens according to their weight. Each chewable flavored tablet is formulated to provide a minimum spinosad dosage of 22.5 mg/lb (50 mg/kg). Spinosad is a member of the spinosyns class of insecticides, which are non-antibacterial tetracyclic macrolides. Spinosad contains two major factors, spinosyn A and spinosyn D, derived from the naturally occurring bacterium, *Saccharopolyspora spinosa*. Spinosyn A and spinosyn D have the chemical compositions 2-[(6-deoxy-2,3,4-tri-O-methyl- α -L-mannopyranosyl)oxy]13-[[5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione and 2-[(6-deoxy-2,3,4-tri-O-methyl- α -L-mannopyranosyl)oxy]-13-[[5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione, respectively.

Indications:

COMFORTIS kills fleas and is indicated for the prevention and treatment of flea infestations (*Ctenocephalides felis*), for one month, on cats and kittens 14 weeks of age and older and 4.1 pounds of body weight or greater.

Dosage and Administration:

COMFORTIS is given orally once a month, at the minimum dosage of 22.5 mg/lb (50 mg/kg).

Do not use the dosing schedule below when administering COMFORTIS to dogs, as it can result in an overdose.

Dosage Schedule:

Body Weight	Spinosad Per Tablet	Tablets Administered
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	(mg)	
4.1 to 6 lbs	140	One
6.1 to 12 lbs	270	One
12.1 to 24* lbs	560	One

*Cats over 24 lbs should be administered the appropriate combination of tablets.

Administer COMFORTIS with food for maximum effectiveness.

COMFORTIS is a chewable tablet that can be consumed by cats when offered by the owner just prior to or after feeding. Alternatively, COMFORTIS may be offered in food or administered like other tablet medications. COMFORTIS should be administered at monthly intervals.

If vomiting occurs within an hour of administration, redose with another full dose. If a dose is missed, administer COMFORTIS with food and resume a monthly dosing schedule.

Treatment with COMFORTIS 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 COMFORTIS should continue the entire year without interruption.

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

Contraindications:

There are no known contraindications for the use of COMFORTIS.

Warnings:

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

Precautions:

Use with caution with concomitant extra-label use of ivermectin (see ADVERSE REACTIONS).

The safe use of COMFORTIS in breeding, pregnant, or lactating cats has not been evaluated.

Adverse Reactions:

In a well-controlled US field study, which included a total of 211 cats (139 treated with COMFORTIS and 72 treated with an active topical control once a month for 3 treatments), no serious adverse reactions were attributed to the administration of COMFORTIS.

Over the 90-day study period, all observations of potential adverse reactions were recorded. Reactions that occurred at an incidence > 1% within any of the 3 months of

observations are presented in the following table. The most frequently reported adverse reaction in cats was vomiting.

Percentage of Cats (%) with Adverse Reactions

	Month 1		Month 2		Month 3	
	COMFORTIS (n=139)	Active Topical Control (n=72)	COMFORTIS (n=135)	Active Topical Control (n=69)	COMFORTIS (n=132)	Active Topical Control (n=67)
Vomiting	14.4	1.4	14.8	1.4	13.6	4.5
Lethargy	3.6	0.0	0.7	0.0	1.5	1.5
Anorexia	2.2	0.0	0.7	0.0	2.3	1.5
Weight Loss	1.4	0.0	0.0	0.0	3.0	0.0
Diarrhea	1.4	1.4	0.7	2.9	2.3	1.5

Over the 3-month (3-dose) study, vomiting occurred on the day of or the day after at least one dose in 28.1% (39/139) of the cats treated with COMFORTIS and in 2.8% (2/72) of the cats treated with the active topical control. Three of the 139 cats treated with COMFORTIS vomited on the day of or the day after all three doses.

Two cats that received extra-label topical ivermectin on Day -1 of the field study developed lethargy on Day 1 after COMFORTIS administration on Day 0.

For technical assistance or to report suspected adverse drug events, contact Elanco US Inc. at 1-888-545-5973.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/reportanimalae>

Mode of Action:

The primary target of action of COMFORTIS in insects is an activation of nicotinic acetylcholine receptors (nAChRs). Spinosad does not interact with known binding sites of other nicotinic or GABAergic insecticides such as neonicotinides, fiproles, milbemycins, avermectins, and cyclodienes. Insects treated with spinosad show involuntary muscle contractions and tremors resulting from activation of motor neurons. Prolonged spinosad-induced hyperexcitation results in prostration, paralysis, and flea death. The selective toxicity of spinosad between insects and vertebrates may be conferred by the differential sensitivity of the insect versus vertebrate nAChRs.

Effectiveness:

In a well-controlled laboratory study, COMFORTIS began to kill fleas 30 minutes after administration and demonstrated 98% effectiveness within 4 hours. COMFORTIS kills fleas before they can lay eggs. In a separate well-controlled laboratory study, COMFORTIS demonstrated 100% effectiveness on the first day following treatment and >90% effectiveness on Day 30.

If a severe environmental infestation exists, fleas may persist for a period of time after

dose administration due to the emergence of adult fleas from pupae already in the environment.

In a field study conducted in households with existing flea infestations, flea count reductions of 97.5% were observed one month after the first treatment and 99.3% after three monthly treatments with COMFORTIS. Cats with pre-existing signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermatitis, and pruritus as a direct result of eliminating the fleas.

Animal Safety:

In a margin of safety study, COMFORTIS was administered orally to 14-week-old kittens at 1X, 3X, and 5X the upper half (75 – 100 mg/kg) of the therapeutic dose band for six monthly dosing intervals 28 days apart. Vomiting was observed across all groups, but was seen with greater frequency in cats in the treated groups; it did not increase with increasing doses. Loose stool was observed in all but the 3X treatment group. Food consumption was decreased in the 5X female cats. COMFORTIS was not associated with clinically significant changes in hematology, clinical chemistry, coagulation, or urinalysis parameters. Cats administered COMFORTIS once monthly for 6 months in the 3X and 5X dose groups demonstrated cytoplasmic vacuolation, consistent with phospholipidosis, in the liver, lung, and adrenal gland. The long term effects of phospholipidosis are unknown. The administration of COMFORTIS was not associated with any clinically significant, gross necropsy or histopathological changes.

In a well-controlled field study, COMFORTIS was administered safely in conjunction with other frequently used veterinary products, including tapeworm anthelmintics, antibiotics, and an approved heartworm preventative containing ivermectin. Hematology and clinical chemistry values were compared pre- and post-study and were unremarkable.

Storage Information:

Store at 20 to 25°C (68 to 77°F), excursions permitted between 15 to 30°C (59 to 86°F).

How Supplied:

COMFORTIS is available in three tablet sizes for use in cats: 140, 270 or 560 mg. Each tablet size is available in color-coded packages of 6 tablets.

COMFORTIS™ -Dogs

(spinosad)

Chewable Tablets

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

Description:

COMFORTIS (spinosad) is available in five sizes of chewable flavored tablets for oral administration to dogs and puppies according to their weight. Each chewable tablet is formulated to provide a minimum spinosad dosage of 13.5 mg/lb (30 mg/kg). Spinosad is a member of the spinosyns class of insecticides, which are non-antibacterial tetracyclic macrolides. Spinosad contains two major factors, spinosyn A and spinosyn D, derived from the naturally occurring bacterium, *Saccharopolyspora spinosa*. Spinosyn A and spinosyn D have the chemical compositions 2-[(6-deoxy-2,3,4-tri-O-methyl- α -L-mannopyranosyl)oxy]-13-[[5-dimethylamino]tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1H-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione and 2-[(6-deoxy-2,3,4-tri-O-methyl- α -L-mannopyranosyl)oxy]-13-[[5-dimethylamino]-tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-Indaceno[3,2-d] oxacyclododecin-7,15-dione, respectively.

Indications:

COMFORTIS kills fleas and is indicated for the prevention and treatment of flea infestations (*Ctenocephalides felis*) for one month, on dogs and puppies 14 weeks of age and older and 5.0 pounds of body weight or greater.

Dosage and Administration:

COMFORTIS is given orally once a month, at the recommended minimum dosage of 13.5 mg/lb (30 mg/kg).

Do not use the dosing schedule below when administering COMFORTIS to cats, as it can result in an underdosage.

Dosage Schedule:

Body Weight	Spinosad Per Tablet (mg)	Tablets Administered
5 to 10 lbs	140	One
10.1 to 20 lbs	270	One
20.1 to 40 lbs	560	One
40.1 to 60 lbs	810	One
60.1 to 120* lbs	1620	One

* Dogs over 120 lbs should be administered the appropriate combination of tablets.

Administer COMFORTIS with food for maximum effectiveness.

COMFORTIS is a chewable tablet and is readily consumed by dogs when offered by the owner just prior to feeding. Alternatively, COMFORTIS may be offered in food or administered like other tablet medications. COMFORTIS should be administered at monthly intervals.

If vomiting occurs within an hour of administration, redose with another full dose. If a dose is missed, administer COMFORTIS with food and resume a monthly dosing schedule.

Treatment with COMFORTIS 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 COMFORTIS 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.

Contraindications:

There are no known contraindications for the use of COMFORTIS.

Warnings:

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

Serious adverse reactions have been reported following concomitant extra-label use of ivermectin with COMFORTIS (see **POST APPROVAL EXPERIENCE**).

Precautions:

COMFORTIS is for use in dogs and puppies 14 weeks of age and older (see **ANIMAL SAFETY**).

Use with caution in breeding females (see **ANIMAL SAFETY**). Use with caution in dogs with pre-existing epilepsy (see **ADVERSE REACTIONS**). The safe use of COMFORTIS in breeding males has not been evaluated.

Adverse Reactions:

In a well-controlled US field study, which included a total of 470 dogs (330 dogs treated with COMFORTIS and 140 dogs treated with an active control), no serious adverse reactions were observed with COMFORTIS. All reactions were regarded as mild and did not result in any dog being removed from the study.

Over the 90-day study period, all observations of potential adverse reactions were recorded. Reactions that occurred at an incidence > 1% within any of the 3 months of observation are presented in the following table. The most frequently reported adverse reaction in dogs in the COMFORTIS and active control groups was vomiting. The occurrence of vomiting, most commonly within 48 hours after treatment, decreased with repeated doses of COMFORTIS.

Percentage of Dogs (%) with Adverse Reactions

	Month 1		Month 2		Month 3	
	COMFORTIS Chewable Tablets (N=330)	Active Topical Control (N=139 ^a)	COMFORTIS Chewable Tablets (N=282)	Active Topical Control (N=124)	COMFORTIS Chewable Tablets (N=260)	Active Topical Control (N=125)
Vomiting	12.7	12.2	7.8	3.2	5.8	4.8

Decreased Appetite	9.1	5.0	2.8	1.6	1.9	0.8
Lethargy	7.6	5.0	3.5	4.0	1.2	0.8
Diarrhea	6.7	5.0	4.3	0.8	1.2	0.0
Cough	3.9	5.0	0.4	2.4	0.0	0.0
Polydipsia	2.4	1.4	0.7	0.0	0.4	0.0
Vocalization	1.8	0.0	0.4	0.0	0.4	0.0
Increased Appetite	1.5	0.0	0.4	0.8	0.4	0.0
Erythema	1.5	0.0	0.4	0.0	0.4	0.0
Hyperactivity	1.2	1.4	0.0	0.0	0.4	0.0
Excessive Salivation	1.2	0.0	0.4	0.0	0.0	0.0

^a This number (n=139) is less than the total number of dogs in the safety population for the active control group (n=140) because one dog joined the study late and was only dosed at Month 3.

In US and European field studies, no dogs experienced seizures when dosed with COMFORTIS at the therapeutic dose range of 13.5-27.3 mg/lb (30-60 mg/kg), including 4 dogs with pre-existing epilepsy. Four epileptic dogs that received higher than the maximum recommended dose of 27.3 mg/lb (60 mg/kg) experienced at least one seizure within the week following the second dose of COMFORTIS, but no seizures following the first and third doses. The cause of the seizures observed in the field studies could not be determined.

Post Approval Experience (June 2009):

The following adverse reactions are based on post-approval adverse drug event reporting. The adverse reactions are listed in decreasing order of frequency: *vomiting, depression/lethargy, anorexia, ataxia, diarrhea, pruritus, trembling, hypersalivation and seizures.*

Following concomitant extra-label use of ivermectin with COMFORTIS, some dogs have experienced the following clinical signs: *trembling/twitching, salivation/drooling, seizures, ataxia, mydriasis, blindness and disorientation.*

Post approval experience continues to support the safety of COMFORTIS when used concurrently with heartworm preventatives according to label directions.

For technical assistance or to report suspected adverse drug events, contact Elanco US Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/reportanimalae>

Mode of Action:

The primary target of action of COMFORTIS in insects is an activation of nicotinic acetylcholine receptors (nAChRs). Spinosad does not interact with known insecticidal binding sites of other nicotinic or GABAergic insecticides such as neonicotinoids, fiproles, milbemycins, avermectins, and cyclodienes. Insects treated with spinosad show

involuntary muscle contractions and tremors resulting from activation of motor neurons. Prolonged spinosad-induced hyperexcitation results in prostration, paralysis, and flea death. The selective toxicity of spinosad between insects and vertebrates may be conferred by the differential sensitivity of the insect versus vertebrate nAChRs.

Effectiveness:

In a well-controlled laboratory study, COMFORTIS began to kill fleas 30 minutes after administration and demonstrated 100% effectiveness within 4 hours. COMFORTIS kills fleas before they can lay eggs. If a severe environmental infestation exists, fleas may persist for a period of time after dose administration due to the emergence of adult fleas from pupae already in the environment. In field studies conducted in households with existing flea infestations of varying severity, flea reductions of 98.0% to 99.8% were observed over the course of 3 monthly treatments with COMFORTIS. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermatitis and pruritus as a direct result of eliminating the fleas.

Animal Safety:

COMFORTIS was tested in pure and mixed breeds of healthy dogs in well-controlled clinical and laboratory studies. No dogs were withdrawn from the field studies due to treatment-related adverse reactions.

In a dose tolerance study, COMFORTIS was administered orally to adult Beagle dogs at average doses of up to 100 mg/kg once daily for 10 consecutive days (16.7 times the maximum recommended monthly dose).

Vomiting was seen in 5 of 6 treated dogs during the first 6 days of treatment, usually within 2.5 hours of dosing. Treated females lost weight early in the treatment period, but their weights were similar to control dogs by the end of the 24-day study. COMFORTIS was not associated with any clinically significant changes in hematology, blood coagulation or urinalysis parameters; however, mild elevations in ALT occurred in all dogs treated with COMFORTIS. By day 24, ALT values had returned to near baseline levels. Phospholipidosis (vacuolation) of the lymphoid tissue was seen in all dogs treated with COMFORTIS, the long-term effects of which are unknown.

In a margin of safety study, COMFORTIS was administered orally to 6-week-old Beagle puppies at average doses of 1.5, 4.4, and 7.4 times the maximum recommended dose at 28-day intervals over a 6-month period. Vomiting was observed across all groups, including the control. Increased vomiting was observed at elevated doses, usually within 1 hour following administration. Vomiting at all doses decreased over time and stabilized when puppies were 14 weeks of age. The average daily and total weight gains of treated dogs were smaller than control dogs and were dose dependent. COMFORTIS was not associated with clinically significant changes in hematology, clinical chemistry, coagulation or urinalysis parameters. Phospholipidosis (vacuolation) of the lymphoid tissue was seen in some dogs in the 4.4X group and all dogs in the 7.4X group. The long term effects of phospholipidosis are unknown. Treatment with COMFORTIS was not associated with any other clinically significant adverse clinical observations, gross necropsy or histopathological changes.

In a reproductive safety study, COMFORTIS was administered orally to female Beagles at

1.3 and 4.4 times the maximum recommended therapeutic dose every 28 days prior to mating, during gestation, and during a six-week lactation period. No treatment-related adverse effects were noted for conception rates in the dams, or for mortality, body temperature, necropsy, or histopathology findings for the dams or puppies. One dam from each treatment group experienced early pregnancy loss and one additional high dose dam aborted late term. The treated dams experienced more vomiting, especially at one hour post-dose, than the control dams. Puppies from dams treated at 1.3 times the maximum recommended therapeutic dose had lower body weights than puppies from control dams. Although puppy mortality between treated and control dams was not different, the puppies from the treated dams experienced more lethargy (4.4X group only), dehydration, weakness and felt cold to the touch (4.4X group only) than puppies from control dams.

A pilot study without a control group was conducted to analyze milk from three lactating dogs treated with an experimental formulation of spinosad at 1.5 times the maximum recommended dose administered at day 28 of gestation and 24 hours prior to parturition. The data demonstrated that spinosyns were excreted in the milk of these dogs. Mortality and morbidity were greatest in puppies from the dam with the highest spinosyns level in milk. The spinosad milk: reference plasma exposure ratio calculated from this study ranged from 2.2 to 3.5.

In well-controlled field studies, COMFORTIS was administered safely in conjunction with other frequently used veterinary products, such as vaccines, anthelmintics, antibiotics, steroids, flea and tick control products, anesthetics, NSAIDs, antihistamines, alternative/herbal remedies, shampoos, and prescription diets. Changes in hematology, clinical chemistry and urinalysis values were compared pre- and post-study and were unremarkable.

Storage Information:

Store at 20-25°C (68 -77°F), excursions permitted between 15 to 30°C (59 to 86°F).

How Supplied:

COMFORTIS is available in five tablet sizes for use in dogs: 140, 270, 560, 810 or 1620 mg.

Each tablet size is available in color-coded packages of 6 tablets.

Approved by FDA under NADA # 141-277

Manufactured for:

Elanco US Inc.

Greenfield, IN 46140

www.comfortis.com

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Elanco[™]

Revised: August 2020

Information for Cat and Dog Owners

COMFORTIS[™] -Cats

(spinosad)

Chewable Tablets

Your veterinarian has chosen to prescribe COMFORTIS to meet your flea treatment and prevention needs. Controlling fleas is important to the health of your cat. Please read this leaflet, which describes the proper use of COMFORTIS to treat and prevent flea infestations. If you have any questions about this information, please consult your veterinarian. Additional information can be found at www.comfortis.com.

What is COMFORTIS?

COMFORTIS is a chewable, flavored tablet that you give to your cat to kill fleas and prevent flea infestations for one month. COMFORTIS is for monthly use in cats and kittens 14 weeks of age or older and 4.1 pounds of body weight or greater.

Why has my veterinarian prescribed COMFORTIS?

Your veterinarian has provided this medication to either prevent a flea infestation or to treat an existing flea infestation on your cat.

What should I discuss with my veterinarian regarding COMFORTIS for my cat?

Your veterinarian is your cat's healthcare expert and can make the best recommendation for medications for your cat. This includes the prevention and treatment of parasites such as fleas that may cause conditions that include flea allergy dermatitis, anemia, and other flea-related problems. Key points of your discussion may include the following:

- Treatment with COMFORTIS may begin at any time of the year, preferably starting one month before fleas become active and continuing through the end of flea season. In areas where fleas may occur year-round, monthly treatment with COMFORTIS should continue the entire year without interruption.
- If a dose is missed, administer COMFORTIS with food and resume a monthly dosing schedule.
- To minimize the likelihood of flea reinfestation, it is important to treat all animals within a household with an approved flea protection product.
- COMFORTIS is not for use in humans. Like all medications, keep COMFORTIS out of reach of children.
- Make sure your veterinarian is aware of all medications, including over-the-counter (OTC) medications, that you are giving to your cat.

How should I give COMFORTIS to my cat?

Give COMFORTIS with food for maximum effectiveness. COMFORTIS is a chewable tablet that can be consumed by cats when offered just prior to or just after feeding. Alternatively, COMFORTIS may be offered in food or administered like other tablet medications. Give COMFORTIS to your cat once a month. To help you remember the monthly dosing schedule, stick-on labels are included for your calendar.

What if I give more than the prescribed amount of COMFORTIS to my cat?

COMFORTIS has been tested in many types of cats, and no severe adverse reactions have been reported. At elevated dose rates, the most severe adverse reaction observed was increased vomiting and loose stool. In the event of possible overdose, contact your veterinarian, who is the healthcare expert for your cat.

Should I restrict either my cat's activity or contact with my cat after the tablet is consumed?

Since COMFORTIS is an oral formulation, you may maintain normal activities and interactions with your cat.

How quickly will COMFORTIS kill fleas?

In a laboratory study, COMFORTIS started to kill fleas within 30 minutes and killed 100% of the fleas within 24 hours. COMFORTIS kills fleas before they can lay eggs.

Does seeing fleas on my cat mean that the treatment is not working?

COMFORTIS kills fleas before they can lay eggs when used monthly according to the label directions. Remember that all animals in the household should be treated with an approved flea product to help control the flea population. Female fleas that are living on animals produce eggs that fall from the animal into their surroundings. These eggs hatch within a week; larvae then emerge and spin cocoons to become pupae. The entire life cycle can be completed in as little as 3 weeks, with new adult fleas emerging from the pupae to jump onto your cat. Because each female flea can lay up to 50 eggs per day, there is potential for a large build-up of eggs, larvae and pupae, resulting in a constant supply of new adults emerging in the cat's environment.

Regardless of the product used to kill the fleas, the cat can continue to be exposed to the fleas that live in the environment. If these fleas jump onto the cat, they will be killed by COMFORTIS. If you see fleas on your cat within a month after your cat receives COMFORTIS, it is most likely that these are new fleas that have recently emerged from pupae and jumped onto the cat. These new fleas will be killed before they can produce eggs that contaminate the environment.

Is it safe to give my cat COMFORTIS?

COMFORTIS has been demonstrated to be safe in cats when used according to label directions. Safety was shown in cats and kittens 14 weeks of age and older, in multiple laboratory studies and a field study in household cats. The safe use of COMFORTIS in breeding, pregnant, or lactating cats has not been evaluated.

What side effects might occur with COMFORTIS?

Like all medications, sometimes side effects may occur. In some cases, cats vomited after receiving COMFORTIS. If vomiting occurs within one hour of administration, redose with another full dose. Additional adverse reactions observed in studies were lethargy,

decreased appetite, weight loss, and diarrhea.

Can other medications be given while my cat is taking COMFORTIS?

Yes, COMFORTIS has been given safely with a wide variety of products and medications. Your veterinarian should be made aware of all medications, including over-the-counter (OTC) medications, that you are giving to your cat. For heartworm prevention, use products that are specifically prescribed by your veterinarian.

How should COMFORTIS be stored?

Store at 68 to 77°F (20 to 25°C). Temporary periods of time outside of this range between 59 to 86°F (15 to 30°C) are permitted.

If you have questions regarding the use of this product, consult your veterinarian, your cat's healthcare expert. Additional information can be found at www.comfortis.com.

For technical assistance or to report suspected adverse drug events, contact Elanco US Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/reportanimalae>

COMFORTIS™ -Dogs

(spinosad)

Chewable Tablets

Your veterinarian has chosen to prescribe COMFORTIS to meet your flea treatment and prevention needs. Controlling fleas is very important to the health of your dog. Please read this leaflet, which describes the use of COMFORTIS to treat and prevent flea infestations. If you have any questions about this information, please consult your veterinarian. Additional information can be found at www.comfortis.com.

What is COMFORTIS?

COMFORTIS is a chewable, flavored tablet that you give to your dog to kill fleas and prevent flea infestations for one month. COMFORTIS is for monthly use in dogs and puppies 14 weeks of age or older and 5.0 pounds of body weight or greater.

Why has my veterinarian prescribed COMFORTIS?

Your veterinarian has provided this medication to either prevent a flea infestation or to treat an existing infestation on your dog.

What should I discuss with my veterinarian regarding COMFORTIS for my dog?

Your veterinarian is your dog's healthcare expert and can make the best recommendation for medications for your dog. This includes the prevention and treatment of parasites such as fleas that may cause conditions that include flea allergy dermatitis, anemia, and other flea-related problems.

Key points of your discussion may include the following:

- Treatment with COMFORTIS may begin at any time of the year, preferably starting one month before fleas become active and continuing through the end of flea season. In areas where fleas may occur year-round, monthly treatment with COMFORTIS should continue the entire year without interruption.

- If a dose is missed, administer COMFORTIS with food and resume a monthly dosing schedule.
- To minimize the likelihood of flea reinfestation, it is important to treat all animals within a household with an approved flea protection product.
- COMFORTIS is not for use in humans. Like all medications, keep COMFORTIS out of reach of children.

How should I give COMFORTIS to my dog?

Give COMFORTIS with food for maximum effectiveness.

COMFORTIS is a chewable tablet and is readily consumed by dogs when offered by the owner just prior to feeding. Alternatively, COMFORTIS may be offered in food or administered like other tablet medications.

Give COMFORTIS to your dog once a month. To help you remember the monthly dosing schedule, stick-on labels are included for your calendar.

What if I give more than the prescribed amount of COMFORTIS to my dog?

COMFORTIS has been tested in many types of dogs, and no severe adverse reactions have been reported. At elevated dose rates, the most severe adverse reaction observed was increased vomiting. In the event of a possible overdose, contact your veterinarian, who is the healthcare expert for your dog.

Should I restrict either my dog's activity or contact with my dog after the tablet is consumed?

Since COMFORTIS is an oral formulation, you may maintain normal activities and interactions with your dog.

How quickly will COMFORTIS kill fleas?

In a laboratory study, COMFORTIS started to kill fleas within 30 minutes and killed 100% of the fleas within 4 hours. COMFORTIS kills fleas before they can lay eggs.

Does seeing fleas on my dog mean that the flea treatment is not working?

COMFORTIS kills fleas before they can lay eggs when used monthly according to the label directions. Remember that all animals in the household should be treated with an approved flea product to help control the flea population.

Female fleas that are living on animals produce eggs that fall from the animal into their surroundings. These eggs hatch within a week; larvae then emerge and spin cocoons to become pupae. The entire life cycle can be completed in as little as 3 weeks, with new adult fleas emerging from the pupae to jump onto your dog. Because each female flea can lay up to 50 eggs per day there is potential for a large build-up of eggs, larvae and pupae, resulting in a constant supply of new adults emerging in the dog's environment.

Regardless of the product used to kill the fleas, the dog can continue to be exposed to the fleas that live in the environment. When these fleas jump onto the dog, they will be quickly killed by COMFORTIS.

If you see fleas on your dog within a month after your dog receives COMFORTIS, it is most likely that these are new fleas that have very recently emerged from pupae and jumped onto the dog. These new fleas will quickly be killed before they can produce eggs that contaminate the environment.

Is it safe to give my dog COMFORTIS?

COMFORTIS has been demonstrated to be safe in pure and mixed breeds of healthy dogs when used according to label directions. Safety was shown in puppies 14 weeks of age and older and adult dogs in both laboratory studies and clinical field studies. You should discuss the use of COMFORTIS with your veterinarian prior to use if your dog has a history of epilepsy (seizures).

Is it safe to give my breeding dogs COMFORTIS?

Use with caution in breeding females. You should discuss the use of COMFORTIS with your veterinarian prior to use in breeding females. Safe use of COMFORTIS in male dogs intended for breeding has not been evaluated.

What side effects might occur with COMFORTIS?

Like all medications, sometimes side effects may occur. In some cases, dogs vomited after receiving COMFORTIS. If vomiting occurs within an hour of administration, redose with another full dose. During clinical studies, no severe or prolonged vomiting occurred. Additional adverse reactions observed in the clinical studies were decreased appetite, lethargy or decreased activity, diarrhea, cough, increased thirst, vocalization, increased appetite, redness of the skin, hyperactivity and excessive salivation. These reactions were regarded as mild and did not result in any dog being removed from the studies. Since the introduction of COMFORTIS, additional side effects reported are incoordination, itching, trembling and seizures.

Can other medications be given while my dog is taking COMFORTIS?

Yes, COMFORTIS has been given safely with a wide variety of products and medications. Your veterinarian should be made aware of all products that you administered and/or intend to administer to your dog. For heartworm prevention, use products that are specifically prescribed by your veterinarian.

How should COMFORTIS be stored?

Store at 68-77°F (20-25°C). Temporary periods of time outside of this range between 59-86°F (15-30°C) are permitted.

If you have questions regarding the use of this product, consult your veterinarian, your dog's healthcare expert. Additional information can be found at www.comfortis.com.

For technical assistance or to report suspected adverse drug events, contact Elanco US Inc. at 1-888-545-5973.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/reportanimalae>

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Elanco[™]

Revised: August 2020

Principal Display Panel - 140 mg Carton Label

FOR CATS

4.1-6 lbs

FOR DOGS

5-10 lbs

KILLS FLEAS

FAST ACTING

ONCE A MONTH

**6 CHEWABLE
TABLETS**

140 mg

**Comfortis™
(spinosad)**

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

KILLS FLEAS AND PREVENTS INFESTATIONS

For use in dogs and puppies 14 weeks of age and older.

For use in cats and kittens 14 weeks of age and older.

Starts killing fleas
in 30 mins.

Kills fleas before
they can lay eggs

Give with
a meal

APPROVED BY FDA under NADA 141-277

Elanco™



Principal Display Panel - 270 mg Carton Label

FOR CATS
6.1-12 lbs

FOR DOGS
10.1-20 lbs

KILLS FLEAS
 FAST ACTING
 ONCE A MONTH

**6 CHEWABLE
 TABLETS
 270 mg**

**Comfortis™
 (spinosad)**

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

KILLS FLEAS AND PREVENTS INFESTATIONS

For use in dogs and puppies 14 weeks of age and older.

For use in cats and kittens 14 weeks of age and older.

Starts killing fleas
in 30 mins.

Kills fleas before
they can lay eggs

Give with
a meal

APPROVED BY FDA under NADA 141-277

Elanco™



Principal Display Panel - 560 mg Carton Label

FOR CATS

12.1-24 lbs

FOR DOGS

20.1-40 lbs

KILLS FLEAS

FAST ACTING

ONCE A MONTH

6 CHEWABLE

TABLETS

560 mg

**Comfortis™
(spinosad)**

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

KILLS FLEAS AND PREVENTS INFESTATIONS

For use in dogs and puppies 14 weeks of age and older.

For use in cats and kittens 14 weeks of age and older.

Starts killing fleas
in 30 mins.

Kills fleas before
they can lay eggs

Give with
a meal

APPROVED BY FDA under NADA 141-277

Elanco™



Principal Display Panel - 810 mg Carton Label

**FOR DOGS
40.1-60 lbs**

**KILLS FLEAS
FAST ACTING
ONCE A MONTH**

**6 CHEWABLE
TABLETS
810 mg**

**Comfortis™
(spinosad)**

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

KILLS FLEAS AND PREVENTS INFESTATIONS

For use in dogs and puppies 14 weeks of age and older.

Starts killing fleas
in 30 mins.

Kills fleas before
they can lay eggs

Give with
a meal

APPROVED BY FDA under NADA 141-277

Elanco™



Principal Display Panel - 1620 mg Carton Label

FOR DOGS
60.1-120 lbs

KILLS FLEAS

FAST ACTING

ONCE A MONTH

**6 CHEWABLE
TABLETS
1620 mg**

**Comfortis™
(spinosad)**

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

KILLS FLEAS AND PREVENTS INFESTATIONS

For use in dogs and puppies 14 weeks of age and older.

Starts killing fleas
in 30 mins.

Kills fleas before
they can lay eggs

Give with
a meal

APPROVED BY FDA under NADA 141-277

Elanco™



COMFORTIS

spinosad tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:58198-0071
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Spinosad (UNII: XPA88EAP6V) (Spinosad - UNII:XPA88EAP6V)	Spinosad	140 mg

Product Characteristics

Color	brown (Brown)	Score	no score
Shape	ROUND (Round)	Size	9mm
Flavor	MEAT (MEAT)	Imprint Code	C

Contains**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-0071-1	10 in 1 BOX		
1	NDC:58198-0071-2	6 in 1 CARTON		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141277	05/22/2018	

COMFORTIS

spinosad tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:58198-0072
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Spinosad (UNII: XPA88EAP6V) (Spinosad - UNII:XPA88EAP6V)	Spinosad	270 mg

Product Characteristics

Color	brown (Brown)	Score	no score
Shape	ROUND (Round)	Size	12mm
Flavor	MEAT (MEAT)	Imprint Code	J
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-0072-1	10 in 1 BOX		
1	NDC:58198-0072-2	6 in 1 CARTON		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141277	05/22/2018	

COMFORTIS

spinosad tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:58198-0073
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Spinosad (UNII: XPA88EAP6V) (Spinosad - UNII:XPA88EAP6V)	Spinosad	560 mg

Product Characteristics

Color	brown (Brown)	Score	no score
Shape	ROUND (Round)	Size	16mm
Flavor	MEAT (MEAT)	Imprint Code	L
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-0073-1	10 in 1 BOX		
1	NDC:58198-0073-2	6 in 1 CARTON		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141277	05/22/2018	

COMFORTIS

spinosad tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:58198-0074
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Spinosad (UNII: XPA88EAP6V) (Spinosad - UNII:XPA88EAP6V)	Spinosad	810 mg

Product Characteristics

Color	brown (Brown)	Score	no score
Shape	ROUND (Round)	Size	18mm
Flavor	MEAT (MEAT)	Imprint Code	C
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-0074-1	10 in 1 BOX		
1	NDC:58198-0074-2	6 in 1 CARTON		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141277	05/22/2018	

COMFORTIS

spinosad tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:58198-0075
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Spinosad (UNII: XPA88EAP6V) (Spinosad - UNII:XPA88EAP6V)	Spinosad	1620 mg

Product Characteristics

Color	brown (Brown)	Score	no score
Shape	ROUND (Round)	Size	22mm
Flavor	MEAT (MEAT)	Imprint Code	J
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-0075-1	10 in 1 BOX		
1	NDC:58198-0075-2	6 in 1 CARTON		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141277	05/22/2018	

Labeler - Elanco US Inc. (966985624)

Establishment

Name	Address	ID/FEI	Business Operations
Elanco SAS France		736833104	MANUFACTURE, ANALYSIS

Establishment

Name	Address	ID/FEI	Business Operations
Eurofins Pharma Quality Control		291433006	ANALYSIS

Establishment

Name	Address	ID/FEI	Business Operations
Eurofins Lancaster Laboratories, Inc		069777290	ANALYSIS

Establishment

Name	Address	ID/FEI	Business Operations
Elanco Clinton Laboratories		039138631	ANALYSIS, LABEL, PACK

Establishment

Name	Address	ID/FEI	Business Operations
Corteva Agriscience LLC		837038785	API MANUFACTURE

Revised: 7/2021

Elanco US Inc.