

McKeever Dermatology Clinics

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NexGard (Merial)

- Treats and prevents flea infestation. Treats and controls Black-legged tick, American Dog tick, Lone Star tick, Brown dog tick.
- Active ingredient:
 - Afoxolaner
- Mode of action:
 - Member of the isoxazoline family
 - Binds to the GABA neurotransmitter and inhibits the ligand-gated chloride channels
 - blocking the pre- and post-synaptic transfer of chloride ions across the cell membrane
 - Causes uncontrolled activity of the CNS and death of the insects
- Effectiveness:
 - Begins to kill fleas four hours after initial administration and has >99% effectiveness after eight hours
 - Fleas are killed before they are able to produce eggs, preventing subsequent flea infestations after the start of treatment
- Dosage:
 - Based on weight
 - Minimum 1.14mg/lb
 - *See table in link attached
- Administration:
 - Can be given with or without food
 - If suspicious any of the dose has been lost or if vomiting occurs within 2 hours of administration, redose with another full dose
 - If a dose is missed, administer NexGard and resume a monthly dose schedule
- Contraindications:
 - None
- Precautions:
 - Safety in pregnant, breeding, or lactating dogs has not been evaluated
 - NexGard should not be given to dogs with a history of seizures
 - seizures were observed after each administration of NexGard in dogs with a history of seizures.
- Adverse Reactions:
 - No serious reactions
 - Most frequent reaction is vomiting
 - generally self limiting and of short duration
 - tends to decrease with subsequent dosing

- *See table in attached link
- Animal Safety:
 - no clinically relevant effects related to treatment on PE, body weight, food consumption, pathology, histopathology, or organ weights
 - Vomiting occurred throughout the study.
 - **No adverse reactions occurred with other medications
 - tested with vaccines, anthelmintics, antibiotics, steroids, NSAIDS, anesthetics, and antihistamines.

http://www.nexgardfordogs.com/Style%20Library/nexgard/docs/NexGard_PI.pdf

Comfortis (Elanco)

- Cats
 - Kills, prevents and treats flea infestation
 - Active ingredient:
 - Spinosad
 - Mode of action:
 - Activates nicotinic acetylcholine receptors
 - involuntary muscle contractions and tremors
 - Does not interact with binding sites of other nicotinic or GABAergic insecticides
 - Effectiveness:
 - Begins killing at 30 minutes and 98% effective in 4 hours
 - 100% effectiveness on the first day and 90% effective on day 30
 - In households with an infestation, flea counts were reduced by 97.5% in one month after first treatment and >90% on day 30
 - Dosage:
 - Based on weight
 - Minimum of 22.5 mg/lb
 - *See dosage chart in link attached
 - Administration:
 - Give with food
 - If vomiting occurs within an hour, administer another full dose
 - If a dose is missed, administer Comfortis and resume a monthly schedule
 - For best results, start 1 month before flea season
 - Contraindications:
 - None
 - Precautions:
 - Use caution with concomitant extra-label use of ivermectin
 - 2 cats on ivermectin developed lethargy a day after Comfortis administration
 - Safety in pregnant, breeding, or lactating cats has not been evaluated
 - Adverse reactions:
 - No serious adverse reactions

- The most frequent adverse reaction is vomiting
 - usually occurred day of or the day after
 - *See link provided for table of reactions
 - Animal Safety:
 - Kittens given doses at the 1X, 3X, and 5X
 - vomiting observed in all groups but does not increase with increased dosing
 - loose stool in all but the 3X
 - food consumption decreased in the 5X
 - **No adverse reactions occurred with other medications
 - tested with frequently used veterinary products including anthelmintics, antibiotics, and an approved heartworm preventative containing ivermectin

<http://www.elanco.us/labels/Companion-Animals/Comfortis.pdf> (Page 1)

- Dogs
 - Kills fleas and indicated for the prevention and treatment of flea infestations
 - Active ingredients:
 - Spinosad
 - Mode of action:
 - Activates nicotinic acetylcholine receptors
 - does not interact with insecticidal binding sites
 - Effectiveness:
 - Begins to kill fleas 30 minutes after administration
 - 100% effective within 4 hours
 - kills before they can lay eggs
 - In households with infestations, reductions of 98%-99.8% were observed over a 3 month treatment
 - Dogs with flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus
 - Dosing:
 - Based on weight
 - Minimum dosage is 13.5mg/lb
 - *See dosing chart in attached link
 - Administration:
 - Give with food
 - If vomiting occurs within an hour, administer another full dose
 - If a dose is missed, administer Comfortis and resume a monthly schedule
 - For best results, start 1 month before flea season
 - Contraindications:
 - None
 - Precautions:
 - Use caution in breeding females
 - no adverse reactions for contraception rates

- dams experienced more vomiting
- puppies from dams treated with 1.3x the maximum dose had lower body weights, more lethargy, dehydrations, weakness, and felt cold to the touch
- spinosyns are excreted in the milk and the mortality and morbidity are greatest in puppies from the dams treated with spinosyns
- Use caution in dogs with pre-existing epilepsy
 - dogs treated with the therapeutic dose range, including 4 dogs with pre-existing epilepsy, did not experience seizures
 - 4 epileptic dogs that received higher than the max dose of 27.3/mg/lb experienced at least one seizure within the week of the second dose but none after the first or third
- Dogs experienced trembling/twitching, salivation/drooling, seizures, ataxia, mydriasis, blindness and disorientation when using Comfortis with concomitant extra-label use of ivermectin
- Adverse reactions:
 - No serious adverse reactions
 - The most frequent reaction is vomiting
 - occurrence decreased with continued dosing
 - *See table in attached link for full list of reactions
- Animal Safety:
 - Dose tolerance study:
 - vomiting seen in 5 of 6 dogs
 - females lost weight early but were similar to the control at day 24
 - dogs had mild ALT elevations
 - on day 24 they had returned to normal
 - Phospholipidosis of the lymphoid tissue was observed in all dogs
 - Puppies given 1.5x, 4.4x, and 7.4x the therapeutic dose:
 - vomiting was observed across all groups, including the control
 - increased vomiting was observed with increasing dosages
 - vomiting in all doses decreased over time
 - Comfortis was not associated with clinically significant changes in hematology, clinical chemistry, coagulation or urinalysis parameters
 - phospholipidosis of the lymphoid tissue was observed in the 4.4x and 7.4x dogs
 - **no adverse reactions occurred with other frequently used vet products
 - vaccines, anthelmintics, antibiotics, steroids

<http://www.elanco.us/labels/Companion-Animals/Comfortis.pdf> (page 2)

- Topical solution to prevent flea infestations
- ONLY FOR USE ON CATS
- Active ingredient:
 - Spinetoram 11.2%
- Mode of Action:
 - Activates nicotinic acetylcholine receptors
- Effectiveness:
 - Starts killing in 30 minutes
 - Kills 100% of fleas in 12 hours
 - Provides +99.9% flea control
 - 96% efficacy at day 37
- Dosing:
 - One low volume dose treats cats of all sizes over 1.8lbs.
 - One tube is 0.77ml
- Administration:
 - Applied to the skin at the base of the head
 - Applied once monthly
- Side effects:
 - May include signs of application site reactions
 - hair loss
 - hair change
 - erythema
 - inflammation
 - itching
- Comfortis vs Cheristin:
 - Both products offer fast-acting, month-long flea protection for cats. You and your clients can select the option that best suits the cat's particular needs.
 - Cheristin provides the ease of a topical solution for cats that are difficult to pill or for owners who prefer topical applications.
 - Comfortis® (spinosad) tablets also offer an option for clients whose cats are undergoing dermatological treatment or groom excessively, as well as for those clients who have children or other pets in the household. Comfortis is administered orally, so there's no need to isolate or avoid contact with the treated cat.

<http://www.elancovet.com/pdf/cheristin-quick-facts.pdf>

<http://www.elanco.us/labels/Cheristin-Label.pdf>

Trifexis (Elanco)

- Used to prevent Heartworm disease

- Kills fleas and prevent infestations
- Used in the treatment and control of adult hookworm, adult roundworm, and adult whipworm
- Active ingredients:
 - Spinosad
 - Milbemycin oxime
- Mode of action:
 - Spinosad
 - activates nicotinic acetylcholine receptors
 - involuntary muscle contractions and tremors
 - does not interact with binding sites of other nicotinic or GABAergic insecticides
 - Milbemycin oxime
 - binds to glutamate-gated chloride ion channels
 - paralysis
 - may also act by disrupting the transmission of invertebrate neurotransmitters
- Effectiveness:
 - Heartworm
 - 100% effective against induced heartworm infections when administered for 3 consecutive monthly doses
 - 2 consecutive doses is not 100% effective
 - Fleas
 - 100% effective on first day of treatment and at day 30
 - 100% effective after 4 hours
 - kills fleas 30 minutes after administration
 - dogs with flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus
 - Intestinal nematodes
 - >90% effective in removing naturally and induced adult roundworm, whipworm, and hookworm
- Dosing:
 - Given orally once a month
 - Minimum dose of 13.5 mg/lb (30mg/kg) spinosad
 - Minimum dose of 0.2 mg/lb (0.5mg/kg) milbemycin oxime
- Administration:
 - Give with food
 - Observe dog for 1 hour
 - If vomiting occurs within an hour, redose with another full does
 - If a dose is missed, administer a full dose and resume a monthly schedule
- Contraindications:
 - None
- Precautions:
 - Dogs should be tested for existing heartworm
 - Mild, transient hypersensitivity reactions manifest as:
 - labored respiration
 - vomiting

- salivation
 - lethargy
 - this occurs in dogs with a high number of circulating microfilariae
 - result of protein release from dead or dying microfilariae
 - Use caution in breeding females
 - some females did not get pregnant when given doses at 3x and 1x
 - relationship between this and spinosad and milbemycin is unknown
 - females in the 3x group lost weight in the 6-week pre-mating period, control group females gained weight
 - malformations in the 1x group included:
 - cleft palate
 - anophthalmia
 - fused single nares
 - misshapen palate
 - hydrocephalus
 - omphalocele
 - malpositioned testes
 - malformation of the anterior tip of the urinary bladder and umbilical blood vessel
 - patent ductus arteriosus (PDA)
 - malformations in the 3x group included:
 - PDA
 - malformations in the control group:
 - malformation of the sternum
 - PDA
 - malpositioned superior vena cava
 - 6-week old puppies
 - given doses 1.5, 4.4 and 7.4 times the maximum recommended dose for 6 months
 - vomiting was observed across all treatment groups and observed at an increased frequency with increased doses
 - vomiting occurred one hour after administration
 - it stabilized when the puppies reached 14 weeks
- Adverse reactions:
 - No serious adverse reactions
 - Most frequent reaction was vomiting
 - One dog experienced a seizure 2.5 hours after receiving the second dose
 - Dogs experienced trembling/twitching, salivation/drooling, seizures, ataxia, mydriasis, blindness and disorientation when taking spinosad which is an ingredient of Trifexis
 - Four epileptic dogs experienced at least 1 seizure within the week following the second dose of spinosad

Bravecto

Kills adult fleas and is indicated for the treatment and prevention of flea infestations and the treatment and control of tick infestations (black-legged tick, American dog tick, brown dog tick) for 12 weeks in dogs and puppies 6 months or older. Also treats and controls lone star tick infestations for 8 weeks in dogs and puppies 6 months or older.

- Active ingredients:
 - Fluralaner
- Mode of action:
 - Belongs to the class of isoxazoline-substituted benzamide derivatives
 - inhibitor of arthropods nervous system
 - antagonist of ligand-gated chloride channels
- Effectiveness:
 - Killed fleas and Ixodes ricinus ticks and reduced numbers of live fleas and ticks by >98% within 12 hours for 12 weeks
 - 100% effective against adult fleas 48 hours post-infection for 12 weeks
 - >93% effective against Dermacentor variabilis, Ixodes scapularis and Rhipicephalus sanguineus ticks 48 hours post-infection for 12 weeks.
 - >90% effective against Amblyomma americanum 72 hours post-infection for 8 weeks
 - not effective beyond 8 weeks
- Dosing
 - Given every 12 weeks
 - Minimum dose of 11.4 mg/lb (25 mg/kg)
 - Must be given every 8 weeks if looking to prevent Amblyomma americanum
- Administration:
 - Give with food
- Contraindications:
 - None
- Precautions:
 - Not effective for 12 weeks in puppies less than 6 months of age.
 - Not effective against Amblyomma americanum ticks beyond 8 weeks after dosing
 - Margin of safety test:
 - administered to 8 and 9 week old puppies at 1, 3, and 5x the maximum dose for 8 week intervals
 - no clinically-relevant, treatment-related effects on physical exams, body weights, food consumption, clinical pathology, gross pathology, histopathology, or organ weights.
 - diarrhea, mucoid and bloody feces were the most common observations in both treatment and control groups
 - one dog in the 3x group was dull, inappetant, bloody diarrhea, vomiting, and weight loss 5 days after starting treatment
 - one dog in the 1x group vomited food 4 hours after first treatment
 - Reproductive study:

- 3x dose given to intact, reproductively-sound male and female Beagles
 - no clinically-relevant, treatment-related effects on the body weights, food consumption, reproductive performance, semen analysis, litter data, gross necropsy or histopathology
 - abnormal salivation on 17 occasions
 - abnormalities:
 - 7 puppies from 2 dams in the treated group had limb deformity, enlarged heart, enlarged spleen, and/or cleft palate
 - 2 puppies in the control group had inguinal testicels
 - 2 puppies in the treated group had inguinal and cryptorchid testicles
- Bravecto has no adverse reactions with other medications.

http://www.mypet.com/pdfs/bravecto/BRAVECTO_PI_MAH.pdf