



PARASITE PREVENTION
While selamectin has been on the market for decades, it is important to review the updated literature due to extra-label use and emerging infectious concerns.

FOCUS ON

Selamectin Use in Companion Animals

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Selamectin is an avermectin parasiticide with a variety of labeled uses in dogs and cats. It is unique in the avermectin class as it is applied topically and not administered orally. It was developed by Pfizer (now Zoetis) and approved by the U.S. Food and Drug Administration (FDA) in 1999 with the trade names Revolution and Stronghold. The trade name varies by geographic region.¹

Recently, an abbreviated new animal drug application (ANADA) was approved by the FDA for a generic version of selamectin (Senegy).² Senegy is currently distributed by Virbac and available in multiple color-coded tube formulations for dosing based on dog or cat body weight. Several other drug manufacturers have also submitted ANADAs for generic selamectin formulations.

Selamectin belongs to the macrocyclic lactone family, which comprises 2 groups: avermectins and milbemycins.

In November 2018, the FDA approved Revolution Plus (selamectin and sarolaner topical solution; Zoetis, zoetis.com) for use in cats. Revolution Plus is now the most comprehensive feline antiparasitic product on the market with the addition of sarolaner to provide efficacy against 3 different tick species.³

MECHANISM OF ACTION

Selamectin belongs to the macrocyclic lactone family, which comprises 2 groups: avermectins and milbemycins. Members of the avermectin group—such as ivermectin, eprinomectin, and doramectin, as well as selamectin—are structurally related. Avermectins bind to glutamate-gated chloride channels, which causes increased permeability of chloride to neurons and leads to hyperpolarization and ultimately parasite death. Mammals do not have glutamate-gated chloride channels and are thus spared the life-threatening effects of avermectin binding.

However, avermectins, including selamectin, do bind GABA_A receptors present in the central nervous system of mammals. Normally, the intact blood–brain barrier with functional P-glycoprotein (P-gp) protects the GABA_A receptors. P-gp is a transmembrane efflux protein encoded by the *ABCB1* (formerly *MDR1*) gene and it is responsible for actively transporting various

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xenobiotics out of the central nervous system.⁴ However, some dogs have a genetic defect (*ABCB1-1Δ*) that results in nonfunctional P-gp and increased risk for various adverse effects associated with excessive P-gp substrate drug concentrations in the central nervous system (**BOX 1**).⁵ The Washington State University Veterinary Clinical Pharmacology Laboratory genotypes dogs via a blood sample or cheek swab; samples can be submitted via veterinarian, or owners may send samples to the laboratory directly (**vcpl.vetmed.wsu.edu**). Dogs that are homozygous for the *ABCB1-1Δ* mutation therefore cannot be treated with extra-label doses of ivermectin, as may be used for conditions such as demodectic mange. It is important to note that the labeled doses of FDA-approved heartworm prevention products are safe, even in homozygous mutant dogs.

Since selamectin is available only in a topical formulation, it is not as subject to significant oral overdose potential as may be seen with other avermectin products.⁴

EFFICACY

See **TABLE 1** for a summary of the labeled indications for selamectin in dogs and cats.

Various field studies have demonstrated selamectin's efficacy in treating flea infestations,⁷ heartworm disease,⁸ and ear mites in dogs and cats,⁹ as well as sarcoptic mange in dogs.⁹ Another study demonstrated selamectin's efficacy against adult roundworm and hookworm infections in cats.¹⁰ In dogs, Revolution (selamectin) has a label for controlling tick infestations due to *Dermacentor variabilis*.¹¹

As nontraditional pets grow in popularity, veterinarians are faced with treatment decisions in species for which

BOX 1 Breeds With Documented *ABCB1-1Δ* Mutation⁶

- Collies
- Australian shepherds
- Shetland sheepdogs
- Old English shepherds
- German shepherds
- Long-haired whippets
- Silken windhounds
- Mixed-breed dogs

there are little to no pharmacologic data. While extra-label provisions allow veterinarians to select empiric treatments, the lack of data and overall understanding of adverse effect profiles of commonly used drugs can lead to treatment failures or even death. Veterinarians must follow all requirements for extra-label drug use as set forth by the FDA and rely on the limited studies available for the best-informed drug decision making. Several of these studies involving guinea pigs and rabbits are highlighted below.

Guinea Pigs

The most common ectoparasite infesting guinea pigs is the skin mite *Trixacarus caviae*,¹² which causes intense pruritus. However, there is a dearth of feasible topical treatment options for these easily stressed animals. A clinical trial investigating a single topical dose of selamectin versus a one-time subcutaneous injection of ivermectin found that both treatments were successful at eliminating *T caviae* mites. The authors concluded that the convenience of the single topical dose of

TABLE 1 Labeled Indications for Selamectin in Dogs and Cats

INDICATION	DOGS	CATS
Prevention and control of flea infestations (<i>Ctenocephalides felis</i>)	Yes	Yes
Prevention of heartworm disease caused by <i>Dirofilaria immitis</i>	Yes	Yes
Treatment and control of ear mites (<i>Otodectes cynotis</i>)	Yes	Yes
Treatment and control of sarcoptic mange (<i>Sarcoptes scabiei</i>)	Yes	No
Control of tick infestations due to <i>Dermacentor variabilis</i>	Yes	No
Treatment and control of roundworm (<i>Toxocara cati</i>)	No	Yes
Treatment and control of hookworm (<i>Ancylostoma tubaeforme</i>)	No	Yes

Cheyletiella mites, colloquially known as “walking dandruff,” usually cause pruritus, scaling, and subclinical disease in rabbits.

selamectin made it the top treatment modality option.¹³ Based on the study protocol, a single dose of 15 mg/kg is recommended.

Rabbits

Cheyletiella mites, colloquially known as “walking dandruff,” usually cause pruritus, scaling, and subclinical disease in rabbits. These nonburrowing mites are zoonotic, which makes them especially relevant to rabbit owners.¹⁴ However, there are no FDA-approved products labeled for *Cheyletiella* in rabbits; veterinarians must extrapolate dosing of existing parasiticides based on available literature. Like guinea pigs, rabbits are easily stressed, making the ease of administration with selamectin’s topical formulation an important factor when formulating treatment protocols.

A team of researchers in South Korea treated 23 *Cheyletiella*-infested rabbits with a single dose of selamectin at 12 mg/kg and found all rabbits were

mite-free at the end of 5 weeks.¹⁵ A retrospective study of cheyletiellosis treatments in pet rabbits examined medical records for various treatment protocols and divided the rabbits into 3 groups.¹⁶ Rabbits were treated with subcutaneous ivermectin alone, a combination of subcutaneous and oral ivermectin, or topical selamectin. The authors concluded that all 3 protocols were effective and safe for use, although the group receiving the combination of subcutaneous and oral ivermectin trended toward lower efficacy.

Textbooks and formularies may advocate particular products for flea control in rabbits; however, veterinarians must realize there is very little in the literature regarding actual pharmacokinetics and safety. A group of researchers at Kansas State University investigated the pharmacokinetics, efficacy, and adverse effects of 2 selamectin doses (10 mg/kg or 20 mg/kg) on flea-infested New Zealand white rabbits. Based on the flea populations in the rabbits, the study concluded that selamectin was rapidly absorbed transdermally and a dosage of 20 mg/kg applied every 7 days was recommended for treating flea-infested rabbits.¹⁷ While the study provides some evidence as to actual drug concentrations in that particular population of rabbits, there are no data on long-term safety of multiple selamectin applications in rabbits.

REVOLUTION PLUS

Revolution Plus, a selamectin and sarolaner topical solution, provides coverage against a variety of important parasites in cats. **TABLE 2** summarizes how

TABLE 2 Labeled Indications for Revolution and Revolution Plus

INDICATION	REVOLUTION (SELAECTIN)	REVOLUTION PLUS (SELAECTIN AND SAROLANER)
Prevention and control of flea infestations (<i>Ctenocephalides felis</i>)	Yes	Yes
Prevention of heartworm disease caused by <i>Dirofilaria immitis</i>	Yes	Yes
Treatment and control of ear mites (<i>Otodectes cynotis</i>)	Yes	Yes
Treatment and control of sarcoptic mange (<i>Sarcoptes scabiei</i>)	Yes	Yes
Control of tick infestations due to <i>Dermacentor variabilis</i>	Yes	Yes
Treatment and control of roundworm (<i>Toxocara cati</i>)	Yes	Yes
Treatment and control of hookworm (<i>Ancylostoma tubaeforme</i>)	Yes	Yes
Treatment and control of infestation with <i>Ixodes scapularis</i> (black-legged tick)	No	Yes
Treatment and control of infestation with <i>Amblyomma maculatum</i> (Gulf Coast tick)	No	Yes
Treatment and control of infestation with <i>Dermacentor variabilis</i> (American dog tick)	No	Yes

the addition of sarolaner changes the overall product profile. Sarolaner is a member of the isoxazoline class, which also includes fluralaner, afoxolaner, and lotilaner.

Ticks in Cats

Many cat owners mistakenly assume that since their pets reside strictly indoors and groom fastidiously, they are not at risk of tick infestation. Cats are also notoriously difficult to medicate (whether via oral or topical route), and many owners may balk at the idea of a regularly scheduled medication administration date with their cat. Unfortunately, recent data suggest that cats are subject to tick infestations,¹⁸ including ticks that transmit zoonotic diseases, such as the black-legged tick (*Ixodes scapularis* can cause anaplasmosis and Lyme disease), the American dog tick (*Dermacentor variabilis* can cause tularemia and Rocky Mountain spotted fever, both potentially deadly to humans), and the Gulf Coast tick (*Amblyomma maculatum* can cause spotted fever).

In a series of studies funded by Zoetis, researchers experimentally infected cats with *I scapularis*, *D variabilis*, and *A maculatum* and divided the cats into 2 groups: placebo or selamectin plus sarolaner. In one of the studies with *I scapularis* and *D variabilis*, another cohort of cats was treated with selamectin alone. Based on the data from all of the studies, the sarolaner–selamectin combination product was effective against the current tick infestation and prevented reinfestation with all tick species for 4 weeks. Selamectin as a sole agent did not affect *I scapularis* and provided only some efficacy against *D variabilis*.¹⁹

Heartworm Disease in Cats

Heartworm disease represents another treatment challenge for many cat owners. The obstacle does not lie with product availability, as there are many commercially available preventive options; rather, as with ticks, many owners assume that their indoor-only cat is not susceptible and simply opt out or forget to treat their cat.

Feline heartworm disease is more difficult to diagnose than canine heartworm disease, and clinical signs in cats may be mistaken for respiratory or gastrointestinal disease.²⁰ While topical selamectin shields cats and dogs from heartworm disease caused by *Dirofilaria immitis*, there is mounting evidence that there are populations of *D immitis* resistant to conventional macrocyclic lactones in dogs.²¹ The role of macrocyclic lactone

resistance and the relationship to *D immitis* are relatively unknown in cats.²¹ Using an experimentally formulated combination of topical selamectin and sarolaner, researchers employed by Zoetis assessed the efficacy of various dosing regimens against a macrocyclic lactone–resistant strain of *D immitis*. One dose of selamectin alone or selamectin plus sarolaner was incompletely efficacious at preventing the development of a macrocyclic lactone–resistant strain of *D immitis* in this population of cats; however, administering the selamectin and sarolaner combination product for 3 consecutive monthly doses was 100% efficacious.²¹ Ultimately, adding sarolaner to the already commercially available selamectin product did not impede selamectin’s ability to prevent heartworm disease in cats, and this study provides another perspective for veterinarians making drug recommendations for their feline patients.

CONCLUSION

While selamectin has been on the market for the past 20 years, its daily use has evolved thanks to new studies, popular pocket pets, and emerging infectious concerns. As always, veterinarians using drugs in an extra-label manner must adhere to the FDA requirements as set forth by the Animal Medicinal Drug Use Clarification Act and diligently assess the literature for pertinent updates. New product options represent exciting new tools in the crusade against parasites in companion animals. **TVP**

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Selarid™ (selamectin)

Topical Parasiticide For Dogs and Cats

BRIEF SUMMARY:

See Package Insert for full Prescribing Information

CAUTION:

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

INDICATIONS:

Selarid is recommended for use in dogs six weeks of age or older and cats eight weeks of age and older for the following parasites and indications:

Dogs:

Selarid kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations. Selarid also is indicated for the treatment and control of sarcoptic mange (*Sarcoptes scabiei*) and for the control of tick infestations due to *Dermacentor variabilis*.

Cats:

Selarid kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (*Ctenocephalides felis*), prevention of heartworm disease caused by *Dirofilaria immitis*, and the treatment and control of ear mite (*Otodectes cynotis*) infestations. Selarid is also indicated for the treatment and control of roundworm (*Toxocara cati*) and intestinal hookworm (*Ancylostoma tubaeforme*) infections in cats.

WARNINGS:

Not for human use. Keep out of the reach of children.

In humans, Selarid may be irritating to skin and eyes. Reactions such as hives, itching and skin redness have been reported in humans in rare instances. Individuals with known hypersensitivity to Selarid should use the product with caution or consult a health care professional. Selarid contains isopropyl alcohol and the preservative butylated hydroxytoluene (BHT). Wash hands after use and wash off any product in contact with the skin immediately with soap and water. If contact with eyes occurs, then flush eyes copiously with water. In case of ingestion by a human, contact a physician immediately. The safety data sheet (SDS) provides more detailed occupational safety information. For a copy of the SDS or to report adverse reactions attributable to exposure to this product, call 1-866-591-5777. Flammable - Keep away from heat, sparks, open flames or other sources of ignition.

Do not use in sick, debilitated or underweight animals (see SAFETY).

PRECAUTIONS:

Prior to administration of Selarid, dogs should be tested for existing heartworm infections.

At the discretion of the veterinarian, infested dogs should be treated to remove adult heartworms. Selarid is not effective against adult *D. immitis* and, while the number of circulating microfilariae may decrease following treatment, Selarid is not effective for microfilariae clearance.

Hypersensitivity reactions have not been observed in dogs with patent heartworm infections administered three times the recommended dose of selamectin solution. Higher doses were not tested.

ADVERSE REACTIONS:

Pre-approval clinical trials:

Following treatment with selamectin solution, transient localized alopecia with or without inflammation at or near the site of application was observed in approximately 1% of 691 treated cats. Other signs observed rarely (<0.5% of 1743 treated cats and dogs) included vomiting, loose stool or diarrhea with or without blood, anorexia, lethargy, salivation, tachypnea, and muscle tremors.

Post-approval experience:

In addition to the aforementioned clinical signs that were reported in pre-approval clinical trials, there have been reports of pruritus, urticaria, erythema, ataxia, fever, and rare reports of death. There have also been rare reports of seizures in dogs (see WARNINGS).

SAFETY:

Selamectin solution has been tested safe in over 100 different pure and mixed breeds of healthy dogs and over 15 different pure and mixed breeds of healthy cats, including pregnant and lactating females, breeding males and females, puppies six weeks of age and older, kittens eight weeks of age and older, and ivermectin-sensitive collies. A litter, estimated to be 5-6 weeks old (0.3 kg), died 89 hours after receiving a single treatment of selamectin solution at the recommended dosage. The litter displayed clinical signs which included muscle spasms, salivation and neurological signs. The litter was a stray with an unknown history and was malnourished and underweight (see WARNINGS).

DOGS: In safety studies, selamectin solution was administered at 1, 3, 5, and 10 times the recommended dose to six-week-old puppies, and no adverse reactions were observed. The safety of selamectin solution administered orally also was tested in case of accidental oral ingestion.

Oral administration of selamectin solution at the recommended topical dose in 5- to 8-month-old beagles did not cause any adverse reactions. In a pre-clinical study selamectin was dosed orally to ivermectin-sensitive collies. Oral administration of 7.5, 10, and 15 mg/kg in this dose escalating study did not cause any adverse reactions; however, eight hours after receiving 5 mg/kg orally, one ivermectin-sensitive collie became ataxic for several hours, but did not show any other adverse reactions after receiving subsequent doses of 10 and 15 mg/kg orally. In a topical safety study conducted with ivermectin-sensitive collies at 1, 3 and 5 times the recommended dose of selamectin solution, salivation was observed in all treatment groups, including the vehicle control. Selamectin solution also was administered at 3 times the recommended dose to heartworm infected dogs, and no adverse effects were observed.

CATS: In safety studies, selamectin solution was applied at 1, 3, 5, and 10 times the recommended dose to six-week-old kittens. No adverse reactions were observed. The safety of selamectin solution administered orally also was tested in case of accidental oral ingestion. Oral administration of the recommended topical dose of selamectin solution to cats caused salivation and intermittent vomiting. Selamectin solution also was applied at 4 times the recommended dose to patent heartworm infected cats, and no adverse reactions were observed.

In well-controlled clinical studies, selamectin solution was used safely in animals receiving other frequently used veterinary products such as vaccines, anthelmintics, antiparasitics, antibiotics, steroids, collars, shampoos and dips.

STORAGE CONDITIONS: Store below 86°F (30°C).

HOW SUPPLIED: Available in seven separate dose strengths for dogs and cats of different weights (see **DOSEAGE**). Selarid for puppies and kittens is available in cartons containing 3 single dose applicators.

Selarid for cats and dogs is available in cartons containing 6 single dose applicators. Approved by FDA under ANADA # 200-663

Manufactured by
Norbrot Laboratories Limited
Newry, BT35 6PU, Co. Down,
Northern Ireland

Revised Dec 2019



FOCUS ON ■ PEER REVIEWED

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