

# Efficacy and Safety of Selamectin (Stronghold<sup>®</sup>/Revolution<sup>™</sup>) Used Off-Label in Exotic Pets

Maggie Fisher, DVM, DipLEVPC<sup>1</sup>  
Wieland Beck, DVM, DipLEVPC<sup>2</sup>  
Melanie J. Hutchinson, DVM<sup>1</sup>

<sup>1</sup>*Shernacre Cottage  
Malvern, UK*

<sup>2</sup>*Institute for Comparative Tropical Medicine and Parasitology  
Faculty of Veterinary Medicine  
Ludwig-Maximilians-University Munich  
Munich, Germany*

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## ABSTRACT

Selamectin, a novel avermectin compound, is reviewed and discussed for its efficacy against naturally occurring infestations and infections of *Ctenocephalides felis*, *Otodectes cynotis*, and *Dirofilaria immitis* in ferrets; different flea species, *Psoroptes cuniculi*, *Cheyletiella* spp, and *Leporacarus gibbus* in rabbits; different chewing lice, *Trixacarus caviae*, and *Chirodiscooides caviae* in guinea pigs; *Ornithonyssus bacoti* and *Demodex* spp in hamsters and gerbils; *Polyplax* spp and fur mites in rats and mice; different flea species, *Demodex erinacei*, *Crenosoma striatum*, and *Capillaria* spp in hedgehogs; and chewing lice in birds. The efficacy and safety of selamectin used off-label in exotic pets are detailed and discussed in this paper. Practical experiences and results suggest that selamectin is effective against a variety of ecto- and endoparasites.

## INTRODUCTION

Selamectin as a spot-on formulation (Stronghold<sup>®</sup>/Revolution<sup>™</sup>, Pfizer Ltd) received marketing authorisation from the European Agency for the Evaluation of Medicinal

Products (EMA) on 25 November 1999 as the first endectocide for use in dogs and cats in Europe. The commercial formulation of selamectin has label claims for the treatment of otodectic mange caused by *Otodectes cynotis* in dogs and cats and for sarcoptic mange due to *Sarcoptes* infestation in dogs. It also has claims against fleas and biting lice in dogs and cats, *Toxocara* spp in dogs and cats, and hookworms in cats. It is licensed as a heartworm preventative with efficacy against larval stages of *Dirofilaria immitis*. Thus, the commercial formulation of selamectin offers small animal practitioners an effective treatment for some common, troublesome parasitic conditions of cats and dogs.

The care of companion animals including exotic pets other than dogs and cats is also the responsibility of the small animal veterinary surgeon, and whilst dogs and cats remain the main pets throughout Europe, there is an upsurge in ownership of pets other than dogs and cats. This is not the first time that more exotic species have been kept as pets; indeed, in eighteenth century Paris, the keeping of exotic animals as household pets was not uncommon.<sup>1</sup> What perhaps is different on this occasion is the importance

being given by veterinarians to the understanding and appropriate treatment of diseases acquired by these animal species. As in other species, ecto- and endoparasites are important causes of disease, ectoparasites being the most common cause of dermatoses in small mammals, except chinchillas.<sup>2,3</sup>

Because there are few medicines licensed for the treatment of pets other than dogs or cats, practitioners often turn to off-label use of products that are available for the treatment of other species. Selamectin has proved to be no exception as, following approval and becoming widely available across Europe, it has been used for the treatment of a broad range of hosts. This is legitimate under the cascade whereby veterinary surgeons can use a product without a label claim in non-food producing animals when there is no suitable product for that indication in that host.<sup>4</sup> This paper reviews the published data on selamectin use in pets other than dogs and cats.

## FERRETS

### Fleas

Flea infestations in ferrets are usually due to the cat flea, *Ctenocephalides felis*<sup>5,6</sup> (Figure 1), and clinical signs are similar to those seen in cats and dogs.<sup>7,8</sup> In a clinical trial, ferrets were treated topically with selamectin at either 6 or 18 mg/kg body weight monthly for 4 months. These ferrets were experimentally infested with fleas 4, 11, 25, and 18 days after each treatment, with surviving fleas being counted 3 days later. Both doses were 100% effective for between 7 and 21 days post-treatment.<sup>9</sup> Moorman-Roest<sup>8</sup> successfully controlled flea infestation in ferrets utilizing monthly applications of 15-mg selamectin per ferret, regardless of weight.

### *Otodectes cynotis*

Otoacariasis in the ferret is caused by the ear mite *Otodectes cynotis*. Clinical signs include a brown waxy exudate from the external ear canal, intense aural irritation, head-shaking, and scratching at the ears.<sup>6,8</sup> In severe infestations, secondary bacterial infections, self-excoriation, eczema, aural

haematomas, and torticollis may result.<sup>10</sup> Because of the anatomical characteristics of the ear of the ferret, conventional treatment involving instillation of drops is of very limited efficacy. A single topical application of approximately 15-mg selamectin per ferret has been reported to be highly effective in the treatment of this irritant infestation.<sup>8,11,12</sup>

## Nematodes

### *Dirofilaria immitis*

*Dirofilaria immitis*, the heartworm, is a filarial nematode infecting dogs, cats, ferrets, and occasionally humans. It is transmitted by the bite of an infected mosquito that transfers infective third stage larvae to the new host when it takes a blood meal. Clinical signs associated with the adult parasite, found primarily in the pulmonary artery, are associated with interference with heart function and pulmonary hypertension.<sup>13</sup> Clinical signs include dyspnoea, cough, pale mucous membranes, lethargy, dehydration, and anorexia.<sup>14,15</sup> Oedema, ascites, and pulmonary congestion may be seen.<sup>14</sup> If untreated, *D immitis* infection may lead to death<sup>14</sup> and as few as 5 adult worms may be fatal to a ferret.<sup>16</sup>

Control in endemic areas is based on prophylactic treatments to eliminate the third and fourth stage larvae before they begin to migrate towards the heart, as treatment and subsequent death of adult worms may result in pulmonary thromboembolism.<sup>13</sup> In a clinical trial, 10 ferrets were treated topically with either 6 or 18 mg/kg body weight selamectin monthly for 4 months. Ferrets were inoculated with *D immitis* larvae 30 days prior to the first treatment. Efficacy of treatment was assessed 24 days after the fifth dose, 173 days post inoculation. Selamectin was 99.5% effective in preventing heartworm infection at a dose rate of 6 mg/kg and 100% effective at a dose rate of 18 mg/kg body weight.<sup>9</sup> Kramer et al<sup>12</sup> report use of selamectin in ferrets without problems at a dose of 18 mg/kg body weight monthly for heartworm prevention.

**Figure 1.** The cat flea (*Ctenocephalides felis*).



## **RABBITS**

### **Fleas**

Domesticated rabbits can be infested by the cat flea *Ctenocephalides felis*, by *Spilopsyllus cuniculi* where there is contact with wild rabbits,<sup>17,18</sup> and by *Pulex irritans*, *Echidnophaga gallinacean*, or *Nosopsyllus fasciatus*.<sup>7</sup> Infestation may be asymptomatic, or a hypersensitivity reaction to flea bites may develop, with alopecia resulting from scratching and biting,<sup>5</sup> resulting in a pruritic papular dermatitis.<sup>7</sup> Van Praag<sup>19</sup> recommends a single topical dose of selamectin at a dose rate of 18 mg/kg body weight for flea control with a repeated treatment 30 days later if required.

### **Mites**

#### ***Psoroptes cuniculi***

*Psoroptes* mites are cosmopolitan ectoparasites of several mammalian hosts. The ear mite, *Psoroptes cuniculi*, mainly affects rabbits and is a common cause of otitis externa (Figure 2). Clinical signs include inflam-

mation, crusting, ceruminous exudate of the ear canal with excoriation of pinnae due to scratching, head shaking, and, in severe infestations, torticollis due to secondary bacterial infection.<sup>7,20-22</sup> In addition, the mites can spread to the body of the host causing a pruritic, crusting dermatitis of the head and neck<sup>18</sup> and ventral abdomen and urogenital region.<sup>7</sup>

The efficacy and safety of selamectin was assessed in rabbits naturally infested with *Psoroptes cuniculi* by McTier et al.<sup>23</sup> Selamectin was applied onto the skin at the base of the neck to give a minimum dose-rate of 6 or 18 mg/kg body weight, either once or twice at 28 days apart. No live mites were recovered from any selamectin-treated rabbit from Day 7 up to 56 days after treatment, while all placebo treatment rabbits remained heavily infested with viable ear mites. In a case study,<sup>24</sup> a 4-month-old male dwarf rabbit and its 3 cage mates diagnosed with *Psoroptes cuniculi* infection were treated with a single dose of 15 mg selamectin. Within

Figure 2. A rabbit with ear canker due to *Psoroptes cuniculi*.



Figure 3. The fur mite of rabbits (*Cheyletiella parasitovorax*).



1 week after treatment, no ear mites were detected. Beck<sup>11</sup> recommends treatment of *Psoroptes cuniculi* in rabbits with selamectin, applying a single dose of 15 or 30 mg, depending on body weight of the animal.

### **Cheyletiella spp**

*Cheyletiella* mites are commonly found on rabbits and are thought to be a normal commensal.<sup>7,25</sup> *Cheyletiella parasitovorax* (Figure 3) is the species associated with the rabbit, but members of the genus *Cheyletiella* are not considered host specific.<sup>26</sup> A common clinical description of *Cheyletiella* infestation is of “walking dandruff,” describing the effect of the movement of the relatively large mites amongst the many skin scales shed into the coat resulting from a heavy infestation.<sup>27</sup> Other signs are variable and include pruritic dermatitis and alopecia.<sup>11,28</sup> Infection is highly contagious and spreads through direct transmission or via fomites and is zoonotic.<sup>27</sup> Human infection is commonly associated with a papular, pruritic rash, often on the forearms<sup>7,18,29</sup> following close contact with the infested pet.

Beck<sup>11</sup> recommends treatment of cheyletiellosis in rabbits with selamectin, applying a single dose of 15 or 30 mg, dependent on body weight, to the skin of the neck. Hughes<sup>19</sup> recommends treatment with selamectin, 15 mg for rabbits weighing less than 2.3 kg and 45 mg for those weighing more than 2.3 kg, with a second treatment 1 month after to kill emerging larvae. A 5-month-old rabbit diagnosed with cheyletiellosis and *Pasteurella* spp infection was treated with selamectin at a dose of 6 mg/kg body weight topically, 2 treatments 14 days apart.<sup>28</sup> Reduced clinical signs were observed within 1 week of treatment and were much improved by 1 month after initial treatment. However the rabbit died suddenly of unknown cause, 22 days after the second treatment.<sup>28</sup>

### **Leporacarus gibbus**

The fur mite, *Leporacarus gibbus*, is a cosmopolitan species and is often found in the fur of rabbits.<sup>25</sup> It is thought to be a commensal ectoparasite, asymptomatic in

normal healthy adult animals.<sup>25</sup> However, in heavy infestations or where there is underlying disease, alopecia, moist dermatitis, mild scurf, and pruritus may occur.<sup>25</sup> Treatment with selamectin, repeated at monthly intervals until live mites are no longer detected, is recommended by Hughes<sup>18</sup> at the dose rate of 15 mg for rabbits weighing less than 2.3 kg and 45 mg for those weighing more than 2.3 kg.

## **GUINEA PIGS**

### **Lice**

Four species of chewing lice, *Gliricola porcelli*, *Gyropus ovalis*,<sup>7</sup> *Trimenopon hispidum*,<sup>11</sup> and *Trimenopon jenningsi*,<sup>30</sup> are commonly found on guinea pigs, especially those kept in colonies. Although normally asymptomatic, heavy infestations may cause pruritus, scaling and alopecia,<sup>5,10</sup> erythema, and papules, particularly around the ears,<sup>30</sup> with anorexia and even epileptiform seizures in severe cases.<sup>11</sup> Beck<sup>10</sup> recommends 15 mg selamectin for animals weighing less than 800 g body weight and 30 mg for animals heavier than 800 g body weight applied as a spot-on to the skin of the neck.

### **Mites**

#### ***Trixacarus caviae***

Sarcoptiform mange in guinea pigs is caused by the mite *Trixacarus caviae*, which is similar in appearance to *Sarcoptes scabiei* var *canis* but is much smaller.<sup>30</sup> Infestation in pet guinea pigs was first reported by Beresford-Jones et al.<sup>31</sup> Infestations cause intense pruritus, leading to severe self-trauma, with lesions of erythema, papules and hyperkeratosis, alopecia, and lichenification occurring in chronic infestations.<sup>10,30,32</sup> Severely affected or untreated animals may have seizures<sup>10,29</sup> and may die from anorexia.<sup>7</sup> Some animals act as asymptomatic carriers.<sup>7,30</sup>

Beck<sup>10</sup> recommends treatment with selamectin at a dose of 15 mg for animals weighing less than 800 g body weight and 30 mg for animals heavier than 800 g body weight applied as a spot-on to the skin of the neck as a treatment for this highly irritant ectoparasitic infestation.

### *Chirodiscooides caviae*

The fur-mite commonly found on guinea pigs is *Chirodiscooides caviae*. Infestations may be asymptomatic, but a heavy infestation may lead to pruritus, alopecia, erythema, and scaling with increased grooming activity leading to self-trauma and ulcerative dermatitis.<sup>30</sup> Concurrent infestation with *Trixacarus caviae*<sup>7</sup> or lice<sup>30</sup> may occur.

Good results in the treatment of this parasite have been achieved with 2 applications of 12 mg/kg body weight selamectin with a 2-week interval.<sup>30</sup> In a clinical case,<sup>33</sup> a 3-year-old guinea pig with a body weight of 600 g was treated with a single topical application of 30 mg selamectin. Clinical signs improved within 1 week of treatment, and pruritus had ceased within a few days. There were no adverse effects following treatment. For convenience, Beck<sup>10</sup> recommends that small guinea pigs (those weighing less than 800 g body weight) are treated with 15 mg selamectin and those weighing 800 g or more are treated with 30 mg selamectin applied as a spot-on to the skin of the neck.

### HAMSTERS AND GERBILS

#### Mites

##### *Ornithonyssus bacoti*

*Ornithonyssus bacoti*, the blood-sucking tropical rat mite, has a worldwide distribution<sup>7</sup> and is zoonotic.<sup>29,33,34</sup> Fox et al<sup>35</sup> reported the first case of *Ornithonyssus bacoti* found on a pet hamster in the UK in 2002, and Beck<sup>36</sup> reported a case of infestation on 2 pet gerbils in Germany. In the case reported by Fox et al,<sup>35</sup> infestation was asymptomatic; however, in the case published by Beck,<sup>36</sup> the gerbils presented with severe pruritus, excoriations, and unusual grooming behaviour. Heavy infestation may result in anemia and death.<sup>7</sup> Beck<sup>36</sup> treated the gerbils with 1 drop of selamectin from a 15-mg pipette. Seven days after treatment, no mites were found in the hair coat. No adverse effects were seen following treatment. Cleaning and decontamination of the environment is important to prevent re-infestation.<sup>36</sup>

### *Demodex* spp

Demodectic mange caused by *Demodex criceti* and *Demodex aurati* in hamsters<sup>5</sup> and *Demodex meriones* in gerbils<sup>7</sup> is relatively common. Infestation is usually asymptomatic, but scaling and alopecia may develop as a result of underlying chronic debilitating disease.<sup>5</sup> Demodectic mange in hamsters can be treated with selamectin, at a dose rate of 6-18 mg/kg body weight, 1 drop 6% selamectin applied to the skin weekly from a pipette.<sup>37</sup>

### RATS AND MICE

#### Lice

*Polyplax* spp are blood-sucking anopluran lice; *Polyplax serrata* infests both rats and mice whereas *Polyplax spinulosa* infests rats only.<sup>7</sup> Infestation results in pruritus and a scaling dermatosis<sup>7</sup> with excoriation and localised alopecia.<sup>10</sup> If infestations are left untreated, so much blood may be removed from the hosts that anemia and even death may occur.<sup>38</sup> Beck<sup>10,11</sup> recommends selamectin, 1 drop from a 15-mg pipette, for treatment of lice in rats and mice.

#### Mites

*Myocoptes musculus*, *Myobia musculi*, and *Radfordia affinis* are the common fur mites of mice.<sup>5</sup> *Radfordia ensifera* infests rats.<sup>7</sup> Infestation is usually asymptomatic but may result in scaling, crusting, pruritus, excoriation, and alopecia where there is underlying debilitating disease or poor housing conditions.<sup>7,10</sup> *Ornithonyssus bacoti* also infests rats and mice, and Pizzi et al<sup>39</sup> reported an outbreak of *O bacoti* in pet rats in the UK in 2003.

In a clinical trial, mice infested with *M musculi* and *M musculus* were treated with selamectin at either 12 or 24 mg/kg body weight on 2 occasions with a 30-day interval. Evaluation of treatment was made at 15-day intervals following the first treatment up to Day 90. Thirty days after the first treatment, efficacy was 98.8% for the 12-mg/kg group and 89.9% for the 24-mg/kg group. Both treatments were 100% effective by Day 90.<sup>40</sup> Beck<sup>11</sup> suggests treatments

with selamectin, using 1 drop from a 15-mg pipette, for mites in rats and mice.

## HEDGEHOG

### Fleas

A survey conducted in Germany found that hedgehogs were infested with the flea species *Archaeopsylla erinacei*, *Ceratophyllus gallinae*, and *Ctenocephalides felis*.<sup>41</sup> Animals may be heavily infested with fleas and show signs of weakness, anaemia, and pruritus.<sup>10</sup> Beck<sup>11</sup> recommends a single topical application of 30 mg selamectin onto the skin of the hosts' neck or back.

### Mites

#### *Demodex erinacei*

Demodicosis caused by the mite *Demodex erinacei* is rarely seen in hedgehogs. Beck<sup>42</sup> reported a case of a hedgehog with demodicosis and *Trichophyton* spp mycosis. The main clinical sign was severe cranial alopecia. The animal was treated with anti-mycotics and selamectin at a dose of 45 mg as a spot-on. Seven days after treatment, the hedgehog's condition had greatly improved and no mites were observed. Four weeks post-treatment, the animal was completely recovered.

### Nematodes

#### *Capillaria spp and Crenosoma striatum*

Schmäsche et al<sup>43</sup> reported the failure of treatment with selamectin at dose-rates of 6 or 15 mg/kg body weight to remove the lungworms *Capillaria aerophila* and *Crenosoma striatum*, and intestinal *Capillaria* spp.

## BIRDS

### Lice

Chewing lice are commonly found on wild birds<sup>44</sup> and are important ectoparasites of domestic birds and represent many species of biting lice<sup>7</sup>; because they are in constant danger of being eaten by their hosts, they are less sluggish than the species that infest mammals, and they may develop enormous populations.<sup>45</sup> The important species found on domestic birds are *Cuclotogaster heterographus*, *Menacanthus stramineus*, *Lipeurus*

*caponis*, *Goniodes dissimilis*, *Goniodes gigas*, and *Goniocotes gallinae*.<sup>7</sup> They spend their whole life cycle on the bird<sup>7</sup> feeding on skin scales, scabs, feathers, and down.

Beck<sup>44</sup> described the case of a buzzard that was found unable to fly. Clinical examination revealed no injuries, but a heavy infestation of non-speciated lice was diagnosed; the parasites were observed with the naked eye moving on the skin of the bird. Microscopic examination confirmed the presence of lice on the head, neck, back, and underside of the wings. A single 15-mg dose of selamectin was applied topically onto the skin of the neck and within 3 days, all parasites had disappeared and the bird was released back into the wild.

## DISCUSSION

Compounds previously used for the treatment and control of ectoparasites in exotic pets usually involve multiple dosing, which increases the likelihood of owner non-compliance and therefore ineffective treatment. Traditional routes of administration, for example injection, bathing, or instillation of acaricide into the ear canal, can be time-consuming, difficult, distressing, and painful, not to mention the likelihood with some exotics of injury to the veterinarian or technician. The use of selamectin applied as a spot-on formulation on a single occasion for ectoparasite control provides a means of safely and effectively treating animals with minimum stress and a maximum of owner compliance. Stronghold™ is produced in a range of colour-coded single-use pipettes, each providing a defined quantity of selamectin, in a 6% or 12% solution. Depending on the dose required for an exotic animal, treatment may involve administration of all or part of the contents of a pipette; treatment regimens employed in different hosts against various parasites are summarised in Table 1.

The pharmacokinetic profile and efficacy of a topically applied drug that exerts its activity following systemic absorption depends upon the permeability of the skin to which the drug is applied, and the formulation of the topical presentation. Inter-species

**Table 1.** Simplified Treatment Regimens for Use of Selamectin in Exotic Pets

Host Species	Parasite	Dose Rate	Additional Information
Ferret	Fleas ( <i>Ctenocephalides felis</i> )	6-18 mg/kg body weight	Repeat monthly treatments may be required
		15 mg	
	Ear mites ( <i>Otodectes cynotis</i> )	15 mg	Adjust the dose rate for small or young animals
	Heartworm ( <i>Dirofilaria immitis</i> )	18 mg/kg body weight	Prophylaxis: repeat treatment at monthly intervals
Rabbit	Fleas	18 mg/kg body weight	Repeat treatment in 30 days may be required
	Ear mites ( <i>Psoroptes cuniculi</i> )	6-18 mg/kg body weight	
		15 mg	
		30 mg	
Mites ( <i>Cheyletiella</i> spp, <i>Leporacarus gibbus</i> )	15 mg for animals $\geq 2.3$ kg body weight	<i>Cheyletiella</i> spp – Second treatment required after 1 month to kill emerging larvae	
	45 mg for animals $> 2.3$ kg body weight	<i>Leporacarus gibbus</i> – repeat treatment at monthly intervals until mites no longer seen	
Guinea pig	Lice	15 mg for animals $\leq 800$ g body weight	
		30 mg for animals $> 800$ g body weight	
	Mites	15 mg for animals $\leq 800$ g body weight	
		30 mg for animals $> 800$ g body weight	
Hamster and gerbil	Mites	1 drop from a 15-mg pipette	
Rat and mouse	Lice	1 drop from a 15-mg pipette	
	Mites	1 drop from a 15-mg pipette	
Hedgehog	Fleas ( <i>Archaeopsylla erinacei</i> )	30 mg	
	Mites ( <i>Demodex</i> spp)	45 mg	
Bird	Lice	15 mg	

variation in absorption of selamectin has been recognised: it has been shown that the maximum concentration ( $C_{max}$ ) of selamectin in cats is much higher than in dogs, possibly due to the greater transdermal flux rate in cats than in dogs.<sup>46</sup> Comparative data in rats shows that the  $C_{max}$  is reached more slowly than in cats but more quickly than in dogs.<sup>47</sup> Comparative data for most other mammals and birds are not yet available.

Selamectin has a favourable safety profile<sup>48,49</sup> and is well-tolerated by cats and dogs, including ivermectin-sensitive collies.<sup>50</sup> All treatments described in this paper were well-tolerated. One death was reported in a rabbit treated 22 days previously,<sup>28</sup> and this case is reported for completeness, although the authors do not believe that that treatment was a likely cause of death given the time interval between treatment and death.



The development of drug resistance is always a concern as the length of time a product has been marketed increases. Macrocytic lactones for use in companion animals have been available since the early 1990s, and to date there are no published or anecdotal reports of resistance to the target pathogens. However, when formulating parasite control strategies, consideration should be given to combining management and parasitocidal treatment in a manner that effectively controls the parasites without unnecessary parasiticide overuse.

A wide range of ectoparasites on exotic pets have been successfully controlled with selamectin treatment. Most selamectin treatments reported to date have been directed towards the treatment of ectoparasites, despite the evidence that selamectin is efficacious against certain endoparasites that infest exotic species as well as dogs and cats. Numerous parasites can be found in or on small mammals and birds. The macrocyclic lactone endectocide selamectin, approved for use in dogs and cats worldwide, has been shown to be safe and highly effective in extra-label use for a range of ectoparasites and some endoparasites of a variety of small mammals and birds.

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