Field efficacy and safety of Felpreva® (tigolaner, emodepside and praziquantel) spot-on for the treatment of natural ear mite infestations (caused by Otodectes cynotis) and notoedric mange (caused by Notoedres cati) in cats.

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Abstract

The miticide efficacy of a single treatment with Felpreva® spot-on solution for cats (Vetoquinol) was evaluated in two European field studies. One study was conducted in cats naturally infested with Otodectes cynotis. The other study was conducted in cats naturally infested with Notoedres cati. In both studies, the presence of viable mites was confirmed prior to treatment (Day -1/Day 0) and re-evaluated on Day 14 (O. cynotis study) and on Day 28 (both studies). Efficacy was calculated based on the number of viable mites found after treatment. In the O. cynotis study, primary criterion was the percentage of mite-free cats after treatment with Felpreva® compared to a sarolaner/selmectin combination (Stronghold® Plus, Zoetis) as a positive control. In the N. cati study, primary criterion was the difference between arithmetic mean mite counts of cats treated with Felpreva® and cats treated with a placebo formulation (solketal). Secondary criteria in both studies were changes in clinical lesion scores after treatment.

In both studies, all Felpreva®-treated cats were mite-free (100 % parasitological cure) 4 weeks after treatment on Day 28. Signs of mange on Day 28 were clinically improved in all Otodectes cynotis-infested cats (100 %) and clinically cured in all Notoedres cati-infested cats (100 %). There were no records of any adverse events or application site reactions in Felpreva®-treated cats.
Key Words

Tigolaner, ear mites, notoedric mange, *Otodectes cynotis, Notoedres cati*, cat
1. Introduction

After fleas and ticks, infestations with mange mites are probably the most clinically relevant ectoparasites in feline parasitology. Ear mite infestations caused by *Otodectes cynotis* (family *Psoroptidae*) are common and in privately-owned kittens often found at the age of 3 to 6 months (Lefkaditis et al., 2009). Prevalence in semi-domestic, stray and shelter cats is variable and can range anywhere between 2.2 % (Portugal, Duarte et al., 2010;) and 30 % (Spain, Fanelli et al., 2020). *O. cynotis* mites are non-borrowing mite that live in the horizontal and vertical ear canal of their host. The clinical picture of otoacariosis typically includes large amounts of dark brown debris inside the ear canal with variable degree of erythema and pruritus (Miller et al., 2013). Occasionally, ear mites are also found outside the ear, often on the head, feet and tail tip (Bowman et al., 2002; Curtis, 2004). Infested cats are known to present anything from apparently healthy (Sotiraki et al., 2001) to severe signs (Yang and Huang, 2016). *O. cynotis* mites are the most common cause of feline *otitis externa* (Harvey et al., 2001; Jacobson, 2002; Nuttall, 2020, Brame and Cain, 2021). It is estimated that they account for up to 85 % of all *otitis externa* cases in cats (Wall and Shearer, 2001). Ear mites are highly contagious and not very host specific, thus often seen in multi-cat/multi-pet household situations (Nuttall, 2020).

Notoedric mange (feline scabies) caused by *Notoedres cati* (family *Sarcoptidae*) is generally considered a rare disease in cats (Wall and Shearer, 2001), though it is known to appear in epizootics (Miller et al., 2013). Cats living in colonies, breeding facilities or catteries are therefore predisposed (Leone and Han, 2020). Actual prevalence data are scarce. In two studies in stray cats, the prevalence of *N. cati* ranged between of 0.6 % in Israel (Salant et al., 2014) and 2.35 % in Greece (Lefkaditis et al., 2015). It is a highly contagious disease that progressively affects the cat’s health and can be fatal if left untreated (Deplazes et al., 2021). *N. cati* are burrowing mites that live in tunnels in the stratum corneum of the epidermis. Clinical signs in infested cats are pruritus, papules, thick crusts, thickened skin and alopecia. Signs characteristically start at the margins of the pinna of the ear and rapidly spread to the whole ear, face, eyelids and neck. Self-grooming and sleeping in a curled position may extend lesions to the feet and perineum of the cat. Pruritus can be intense, and lesions caused by self-trauma are often observed, which increases the risk for secondary bacterial or yeast infections (Miller et al., 2013; Leone and Han, 2020). If not treated, cats may develop lethargy, dehydration, and weight loss. Death is rare but can occur and is more frequently seen in young kittens and immunosuppressed cats (Bowman et al., 2002; Foley et al., 2016; Leone and Han, 2020).

Felpreva® (Vetoquinol S.A. Lure, France) is a new long-acting spot-on solution for cats using a fixed combination of tigolaner, emodepside and praziquantel. The product was registered in the European Union (EMA, 2021) and possesses broad-spectrum activity against both, endo- and ectoparasites. Previous reports have described the high anthelmintic efficacy of Felpreva® in cats naturally infected with intestinal nematodes, cestodes and lungworms (Cvejic et al., 2022a; Traversa et al., 2022).
Moreover, ectoparasite studies demonstrated a 3-months efficacy in cats naturally infested with ticks and fleas (Cvejic et al., 2022b), a fast onset of flea efficacy (Mencke et al., 2023) and high efficacy in cats infested with paralysis tick *Ixodes holocyclus* (Roebert et al., 2023). More recently, Felpreva® was reported to be highly active against artificial infestations with *O. cynotis* mites (Blazejak et al., 2023). This article aims to continue recent work by presenting the miticidal efficacy in cats naturally infested with *O. cynotis* and *N. cati* mites. Efficacy was assessed in two European field studies. The objective of the two studies reported here, was to demonstrate that a single treatment with Felpreva® is highly effective in eliminating natural infestations with both mange mite species 4 weeks after treatment.

### 2. Material and Methods

Two field studies were conducted, one in cats naturally infested with *O. cynotis* (study #1) and one in cats naturally infested with *N. cati* (study #2). Cats with *O. cynotis* infestations were enrolled in 15 different study sites located in Hungary and Portugal. Cats with *N. cati* infestations were enrolled in one study site in Albania.

Both studies were in compliance with the principles of Good Clinical Practice (EMA, 2000) and following the recommendations of guideline “Demonstration of efficacy of ectoparasiticides” (EMA, 1994). The studies were part of the development program for the regulatory approval of Felpreva®.

#### 2.1 Animals and study design

Cats with clinical signs of otodectic (study #1) or notoedric (study #2) mange were eligible for study inclusion when the presence of viable mites was confirmed pre-treatment.

#### 2.1.1 *Otodectes cynotis* study

The study in *O. cynotis* infested cats was a positive controlled, blinded, randomised, multicenter and multiregional field study with 7 participating veterinary clinics in Portugal and 8 veterinary clinics in Hungary. All cats enrolled in the study were client-owned cats. Eligible households had a maximum of 5 animals (maximum of 3 cats and 2 dogs). One cat per household was nominated as the primary patient for the efficacy and safety evaluations. Other cats of the same household were classified supplementary cats. Supplementary cats received the same treatment as the primary cat and were monitored for safety, but not included in the efficacy evaluations. Dogs living in the same household were treated against ear mites but not included in any efficacy or safety evaluation of the study.

All enrolled cats (primary and supplementary) were clinically healthy on Day 0 (except for confirmed mite infestation), non-pregnant, non-lactating and not treated with any ectoparasiticide with known miticidal efficacy within the last 3 months prior to Day 0. Cats had to be at least 10 weeks old with a
minimum body weight of 1.25 kg. Animal owners gave written consent and allowed their animals to be
treated and managed according to the procedures described in the study protocol.

Physical exams, body weights and assessment of the application site were taken prior to treatment on
Day 0, and again on Day 14 (± 2) and Day 28 (± 2). Presence or absence of ear mites and clinical signs
of ear mite infestation (ear mite lesions) were assessed for both ears of each cat on Day 0 prior to
treatment, and again on Day 14 (± 2) and Day 28 (± 2). Ears were not cleaned after otoscopic
examinations.

Grooming and bathing of the cats was reduced to a minimum during the study and specifically not
permitted within 48 hours after treatment and 48 hours before a scheduled visit.

Blinding was ensured by separation of study roles. Treatments on Day 0 were applied by trained
personnel (dispenser) not involved in diagnosing viable ear mite infestations, assessment of ear mite
lesions or any other clinical observations. All personnel (veterinarians) responsible for the diagnosis and
assessment of mite infestations and lesion scores were blinded to treatment allocations. Animal owners
were also unaware of treatment allocations.

2.1.2 Notoedres cati study

The study in N. cati infested cats was a randomised, blinded, negative-controlled, parallel-group, single
center study which was conducted in Albania. Cats enrolled in this study were client-owned, naturally
infested cats. The animal owners gave written consent prior to study start and allowed their animals to
be treated and managed according to the study protocol procedures. For the duration of the study, all
cats were housed individually in a controlled study facility. Cats were admitted without any
acclimatisation period. During the study, cats were maintained on their usual feed and water routine and
observed daily for general health. After study completion on Day 28, all cats were returned to their
animal owners. Ownership of each cat always remained with their respective owner for the entire study
duration.

Cats were clinically healthy on Day 0 (except for confirmed mite infestation), non-pregnant, non-
lactating and not intended for breeding for a total of 4 months following administration of the study
treatments. None of the cats had had been treated with an ectoparasiticide with known miticidal efficacy
within the last 3 months prior to Day 0. All cats were at least 10 weeks old with a minimum body weight
of 1 kg.

Physical examinations were performed pre-treatment on Day -1 (+1) and Day 0 and again on Day 14
and Day 28. Body weights were measured on Day -1 (+1) and Day 28. Assessments of the application
site were made on Day -1 (+1) and on Day 0 prior to treatment, 4 and 8 hours after treatment and again
on Days 1, 2, 7, 14, 21 and 28. Assessments for the presence of live mites were performed on Day -1
(+1) and on Day 28. Clinical signs of notoedric mange were assessed on Day 0, Day 14 and Day 28.
Blinding was ensured by separation of study roles. Treatments on Day 0 (+1) were applied by personnel not involved in diagnosing viable mite infestations, assessment of notoedric lesions or any other clinical observations. All personnel responsible for the diagnosis and assessment of mite infestation and lesion scores were blinded to treatment allocations. Animal owners were also unaware of treatment allocations.

2.2 Randomisation and treatment administrations

2.2.1 Otodectes cynotis study

Eligible cats were randomised per household in the sequence of inclusion and assigned to one of two treatment groups. Allocations were made using a block design and a 1:1 treatment ratio. Cats were treated topically with a spot-on formulation once on Day 0, either with Felpreva® (Vetoquinol Lure, France) or with Stronghold® Plus (Zoetis Belgium SA). All cats from the same household (primary and supplementary cats) were allocated to the same treatment group. Treatment administration was the responsibility of the assigned study dispenser in each clinic. The appropriate pipette size was selected based on the cat’s pre-treatment body weight, to provide a minimum recommended dose rate of 14.4 mg tigolaner, 3 mg emodepside and 12 mg praziquantel per kg body weight for Felpreva® and a minimum of 6 mg selamectin and 1 mg sarolaner per kg body weight for Stronghold® Plus. Both products were applied according to label instructions directly to the skin at the base of the skull. When dogs were present in the household, these were treated with a marketed oral miticidal product (Bravecto® chewable tablets for dogs, Merck Animal Health).

2.2.2 Notoedres cati study

On Day 0, eligible cats were randomised to treatment groups based on pre-treatment mite counts. Cats were blocked into two groups of cats, one group with > 10 mites/cat and one group with ≤ 10 mites/cat. Within each block, cats were then randomly allocated to Felpreva® or placebo (solketal syn. isopropylidiniglycerol, a glycerol derivative) in a 1:1 treatment ratio. Study treatments were applied once on Day 0.

Cats allocated to Felpreva® were treated at the minimum recommended dose rate of 14.4 mg tigolaner, 3 mg emodepside and 12 mg praziquantel per kg body weight. Cats allocated to placebo received solketal. Dose volumes per kg body weight were the same for both products (0.148 ml/kg body weight). Application volumes were calculated (pre-treatment body weight X dose volume per kg body weight, rounded up to two decimal places) and administered once on Day 0 directly to the skin at the base of skull of each cat.
2.3 Efficacy assessments

2.3.1 Otodectes cynotis study

Presence of Otodectes cynotis (mite counts):

Otoscopic examination and/or microscopic examination of aural canal debris and exudates were used to confirm the presence or absence of live O. cynotis mites (immature and adult stages) in each primary cat. The presence/absence of ear mites was assessed on Day 0 (prior to treatment), on Day 14 and at study completion on Day 28. Mite counts were performed once on Day 0 prior to treatment to ensure that all eligible cats were adequately infested (minimum of 3 live ear mites present in at least one ear).

Clinical signs of Otodectes cynotis infestation (Otodectes-induced ear lesion [OEL] score):

Clinical signs of ear mite infestation were assessed for both ears of each cat on Day 0 prior to treatment, and again on Day 14 and Day 28. Assessments were made using the Otodectes-induced ear lesion (OEL) score. Each cat was assessed for head shaking, pruritus (ear scratching), trauma or alopecia at the pinna, erythema and debris in the ear canal using a scoring system of 0 (absent), 1 (mild), 2 (moderate) or 3 (severe). The sum of all scores for one ear was the OEL score. The ear with the higher OEL score of each cat was used for the efficacy evaluations (Table 1).

2.3.2 Notoedres cati study

Presence of Notoedres cati (mite counts):

Deep skin scrapings on Day -1 and on Day 28 were used to confirm the presence or absence of viable N. cati mites in each cat. Samples from an area of approximately 1 cm² were collected from three different body sites suspected of being mite-infested and examined microscopically. Viable larvae, nymphs and adult mites of all three scrapings were counted and results were summed up to a total number of viable mites. All enrolled cats were mite-positive on Day -1.

Clinical signs of Notoedres cati infestation (Notoedres-induced skin lesions [NISL] score):

Clinical signs of notoedric mange were evaluated on Days -1, Day 14, and Day 28, just before any skin scrapings were taken. Severity of notoedric skin lesions was determined using a scoring system of 0 (no lesions, no alopecia, no scratching) to 3 (severe skin lesions, severe alopecia, intensive scratching). The extent of notoedric skin lesions was determined using a score from 0 (no skin lesions) to 2 (≥ 50 % of the body skin surface involved. The sum of both scores (severity and extent) was the Notoedres-induced skin lesion (NISL) score which was used for the efficacy evaluations (Table 2). All enrolled cats had a minimum NISL score of 1 on Day -1.
2.4 Safety assessments

In both studies, all enrolled cats (including supplementary cats of study #1) were regularly assessed for safety within scheduled or when needed unscheduled study visits. Any sign of abnormal health and any sign at the application site were documented for each cat either observed by the veterinarian (both studies) or reported by the animal owner (study #1).

The application site was assessed in study #1 on Day 0 (before treatment), Day 14 and at study completion on Day 28. In study #2, assessments were made on Day 0 (before treatment and 4 and 8 hours after treatment) and on Days 1, 2, 7, 14, 21 and 28.

2.5 Statistical analysis

All calculations were made in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The experimental unit was the individual (primary) cat in both studies.

2.5.1 Otodectes cynotis study

Efficacy analyses:

Efficacy analyses included data of all primary cats that completed the study per protocol (per protocol population). The presence or absence of live ear mites was summarised by treatment group and study day. The parasitological cure rate, defined as the percentage of mite-free cats in respective treatment group (Felpreva® or Stronghold® Plus) was calculated for Day 14 (secondary efficacy criterion) and Day 28 (primary efficacy criterion). Non-inferiority of the parasitological cure rate for Felpreva®-treated cats compared to Stronghold® Plus-treated cats was assessed for Day 14 (secondary criterion) and Day 28 (primary criterion) using a generalised linear mixed model with fixed treatment effects and random clinic effects. The test was one-sided with a significance level of 2.5 %. Non-inferiority was demonstrated if the lower limit of the 97.5 % confidence interval (CI) of the difference in efficacy between both products was greater than -15 %.

Effect of treatment on OEL scores (secondary criterion) was compared between both treatment groups with the Cochran-Mantel-Haenszel test, adjusted by clinic (reported as risk ratio with a two-sided 95 % confidence interval and 5 % level of significance). Both ears of each cat were scored on each observation day (Days 0, 14 and 28) to identify the ear with the higher score which was then used for treatment effect comparisons. The treatment effect was calculated as the percentage of animals with improved, worsened and with no change in OEL scores in the respective study period (Day 0-Day 14; Day 0-Day 28, Table 1).
Safety analyses:

Safety analyses included data of all primary and supplementary cats (intention to treat population). The percentage of adverse events (non-serious and serious) and the percentage of suspected adverse drug reactions were compared between both treatment groups with a Fisher’s exact test (two-sided 95% confidence interval, 5 % level of significance).

2.5.2 Notoedres cati study

Efficacy analyses:

Efficacy analyses included data of all cats that completed the study per protocol (per protocol population). The total number of viable mite counts on Day 28 was summarised by treatment group. Primary efficacy criterion was the difference of arithmetic mean mite counts between cats in the Felpreva® group and cats in the placebo group. Efficacy (%) was calculated using the Abbott formula: $100 \times (C-T)/C$, where $C$ was the arithmetic mean of viable mite counts of cats in the placebo group and $T$ was the arithmetic mean of viable mite counts of cats in the Felpreva® group. Groups comparisons were made with a test for superiority by applying the one-sided Wilcoxon-Mann-Whitney test with a Mann Whitney (MW) measure of 0.50 (equality) as traditional benchmark.

The treatment effect on NISL scores (secondary criterion) was compared between both treatment groups with the Mantel-Haenszel chi-square statistic (two-sided 95% confidence interval, 5 % level of significance), calculated as the percentage of animals classified as clinically cured, clinically improved or clinical failure on Day 28 compared to Day -1 (Table 2).

Safety analyses:

Safety analyses included data of all cats (intention to treat population). The percentage of adverse events (non-serious and serious), the percentage of suspected adverse drug reactions and the percentage of application site reactions were compared between both treatment groups with Fisher’s exact test (two-sided 95 % confidence interval, 5 % level of significance).

3. Results

3.1 Comparability of treatment groups pre-treatment

Animal baseline characteristics of both studies are displayed in Table 3.
Treatment group comparisons of breed, sex, age, body weight, coat length in the *O. cynotis* study (study #1) demonstrated statistically significant differences on Day 0 in the average age (Felpreva®-treated cats: 28.8 months, Stronghold® Plus-treated cats: 42.7 months, Wilcoxon test, p=0.026, per protocol population) and body weight (Felpreva®-treated cats: 3.0 kg, Stronghold® Plus-treated cats: 3.3 kg, Wilcoxon test p=0.053, per protocol population) on Day 0. These differences however were considered not to be clinically relevant, nor with any impact on the statistical endpoint analysis (parasitological cure). The other parameters (breed, sex, coat length) were comparable between both groups. Both treatment groups had similar OEL scores on Day 0 (Felpreva®-treated cats: 7.53; Stronghold® Plus-treated cats: 7.34).

Animal baseline characteristics, NISL scores and mite counts on Day -1 in the *N. cati* study (study #2) were comparable in both treatment groups (Felpreva®, solketal, per protocol population, data not shown).

### 3.2 Efficacy *Otodectes cynotis* study

A total of 252 cats (157 primary and 95 supplementary cats) were included in the study. 148 primary cats were treated per protocol and included in the efficacy analyses. Data of all 252 cats were assessed in the safety evaluations.

All 148 primary cats (78 Felpreva®-treated cats and 70 Stronghold® Plus-treated cats) were mite-free (100 % efficacy) at study completion on Day 28. A statistical analysis could not be carried out due to missing differences between both treatment groups, but non-inferiority of Felpreva® to Stronghold® Plus was concluded. Efficacy on Day 14 was 89.7 % in Felpreva®-treated cats and 88.6 % in Stronghold® Plus-treated cats (Table 4). Non-inferiority was demonstrated as the lower limit of the 97.5 % CI was greater than pre-defined -15 % (97.5 % CI: -0.09).

OEL scores on Day 14 and Day 28 were similar in both treatment groups and no statistical difference was found. Most treated cats had clinically improved by Day 14. 76 out of 78 (97.4 %) Felpreva®-treated cats and 68 out of 70 (97.1 %) Stronghold® Plus-treated cats showed improved OEL scores on Day 14 (risk ratio 1.0, 95 % CI: 0.95; 1.06, p=0.869). On Day 28, improved OEL scores were found in all 78 (100 %) Felpreva®-treated cats and in 69 out of 70 (98.6 %) Stronghold® Plus-treated cats (risk ratio, 1.01, 95 % CI: 0.99; 1.04, p=0.317) (Figure 1). When clinical improvement was displayed as the course of mean OEL scores from Day 0 to Day 28, both treatment groups (Felpreva®/Stronghold® Plus) presented a similar marked decline in mean scores from Day 0 (7.53/7.34) to Day 14 (2.27/2.51), followed by a further though slower decline until Day 28 (0.85/0.87) (Figure 2).
3.3 Efficacy *Notoedres cati* study

A total of 20 cats (10 Felpreva®-treated cats and 10 placebo-treated cats) were enrolled in the study. All cats completed the study per protocol and were included in efficacy and safety evaluations.

Four weeks after treatment on Day 28, all Felpreva®-treated cats were mite-free (100 % efficacy), whereas an arithmetic mean of 5.5 viable *Notoedres cati* mites was found in in placebo-treated cats.

Superiority of Felpreva® over placebo was concluded (MW = 1.0, 95 % CI: 0.811; 1.189; p≤0.0001) (Table 5).

Clinical signs of notoedric mange (NISL score = 0) were cured in 40 % of Felpreva®-treated cats on Day 14 which increased to 100 % of the cats on Day 28. In comparison, clinical cure of NISL was not seen in any of the placebo-treated cats, neither on Day 14, nor on Day 28. The difference between Felpreva®-treated cats and placebo-treated cats was statistically significant for both days (p=0.029 for Day 14 and p<0.001 for Day 28) (Figure 3).

3.4 Safety observations

In both studies, there were no records of any adverse event or application site reaction in Felpreva®-treated cats.

4. Discussion

Results of the two field studies showed that a single treatment with Felpreva® spot-on solution effectively eliminated all *O. cynotis* and all *N. cati* mites in naturally infested cats 4 weeks after treatment. No adverse reactions were seen in both studies.

The high efficacy of Felpreva® against *O. cynotis* mites presented here is in line with results from earlier dose confirmation studies (Blazejak et al., 2023) where parasitological cure rates in artificially infested cats ranged between 99.6-100 % 4 weeks after administration. In this field study, all Felpreva®-treated cats (100 %) were free of ear mites on Day 28 and almost 90 % of them were already cured by Day 14 demonstrating that *O. cynotis* mites were rapidly and effectively killed after a single application of Felpreva®. It seems likely that the early removal of ear mites from the ear canal had a positive effect on the course of clinical otoacariosis signs suggested by the rapid improvement of post-treatment OEL scores in most of the treated cats. 97.4 % of the Felpreva®-treated cats had clinically improved by Day 14 increasing to 100 % of the cats on Day 28. These results were achieved without any additional measures or medication other than treating in-contact cats and dogs of the same household. Regular cleaning of the cat’s ears, the cat’s surroundings, and house cleaning as it has been traditionally recommended for ear mite-infested pets (Harvey et al., 2001; Wall & Shearer, 2001; Curtis et al., 2004) were not applied in the study.
Treatment with Felpreva® was also highly effective against natural infestations with *N. cati* mites. Four weeks after treatment on Day 28, all Felpreva®-treated cats were mite-free (100 % parasitological cure) and all signs of notoedric mange had resolved (100 % clinical cure) whereas untreated control cats remained infested (mean of 5.5 viable mites) and did not present any clinical improvement (0 % clinical cure; 0 % clinical improvement). Traditional treatment protocols for notoedric mange in cats used to be based on the administration of macrocyclic lactones which, depending on the active, must be applied once or twice at 1-month intervals (moxidectin, eprinomectin) or at least twice every 2 weeks (selamectin, ivermectin, Leone & Han, 2020). Other recommendations include additional weekly lime-sulfur dips or keratolytic shampoos for the treatment of pruritus and to remove skin scales (Schnyder et al., 2019). If necessary, antibiotic and corticosteroid therapy may be applied for severe clinical cases (Bowman et al., 2002). In our study, complete cure (parasitological and clinical) was achieved in Felpreva®-treated cats within 1 month after a single treatment and without any further measures such as regular baths or any other concomitant treatment. It is important to note that severe clinical cases of notoedric mange were not seen in our study. Results of our study are based on cats merely displaying mild to moderate signs of notoedric mange (NILS score 1 and 2) on the day of enrolment.

The acaricidal activity of Felpreva® is determined by tigolaner, a novel GABA antagonist which belongs to the class of bispyrazoles. Tigolaner has insecticidal and acaricidal activity, like the class of isoxazolines. In studies evaluating topical isoxazoline products, parasitological cure rates in cats with natural *O. cynotis* infestations ranged between 97.4 % (esafoxolaner, Nexgard® Combo, Boehringer-Ingelheim Animal Health, Tielemans et al., 2021) and 100 % (fluralaner, Bravecto® spot-on, MSD Animal Health, Bosco et al., 2019) 4 weeks after treatment. 100 % efficacy (based on mite counts) was seen with esafoxolaner in *N. cati*-infested cats on Day 27/28 (Knaus et al., 2021). Results of our studies show that treatment with Felpreva® has equally high efficacy against *O. cynotis* and *N. cati* mites in cats as currently marketed isoxazoline products. In our study, treatment with Felpreva® was statistically non-inferior to a sarolaner/selamectin combination (Stronghold® Plus) when applied to ear mite-infested cats.

This is another report demonstrating the excellent efficacy and safety profile of Felpreva® in cats. In the past, management of otodectic or notoedric mange in cats was laborious and time-consuming and most treatment protocols did not include very feline-friendly procedures. Daily ear cleaning or regular bathing is a traumatic experience for most cats and likely a common reason why pet owners may prematurely cease treatment. The present studies demonstrate that a single treatment with Felpreva® will provide high efficacy against mange mites while offering an easy-to-use medicine with an excellent safety profile for a stress-free management of cats, all characteristics that are likely to enhance owner adherence.
5. Conclusions

A single spot-on administration of Felpreva® was 100% effective in clearing natural *O. cynotis* and *N. cati* infestations in cats 4 weeks after treatment. Clinical signs of otodectic mange were improved and signs of notoedric mange resolved in all treated cats. The topical application of Felpreva® was very well tolerated by all cats.

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