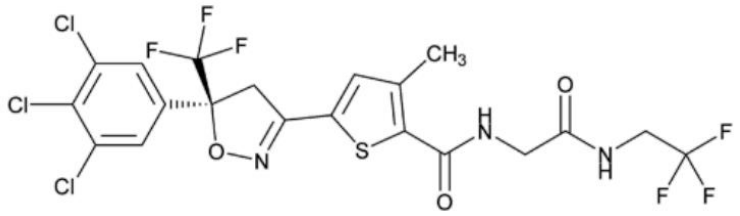
PrCredelio™ CAT
Package Insert

PrCredelio™ CAT
(lotilaner chewable tablets)

FOR VETERINARY USE ONLY

DESCRIPTION
CREDELIO CAT (lotilaner) is an oral, once-a-month, flavoured chewable tablet for cats and kittens. CREDELIO CAT are white to beige round biconvex chewable tablets with brownish spots and beveled edges. The chemical composition and structure are as follows: 5-[(5S)-4,5-dihydro-5-(3,4,5-trichlorophenyl)-5-(trifluoromethyl)-3-isoxazolyl]-3-methyl-N-[2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl]- 2-thiophenecarboxamide.



THERAPEUTIC CLASSIFICATION
Lotilaner is an ectoparasiticide belonging to the isoxazoline class of parasiticides.

INDICATIONS
CREDELIO CAT is indicated for:

1) The treatment and prevention of flea infestations (*Ctenocephalides felis*) for one month in cats and kittens 8 weeks of age and older, weighing 0.9 kg or greater, and as part of a treatment strategy for the control of flea allergy dermatitis (FAD).
2) The treatment and control of *Ixodes scapularis* (black-legged or deer tick) infestations for one month in cats and kittens 6 months of age and older.

DOSAGE AND ADMINISTRATION
CREDELIO CAT chewable tablets are given orally once a month with a dosage of 6 - 24 mg lotilaner/kg bodyweight.
Use the table below to find the right dose for the cat's weight.
Administer CREDELIO CAT with food or after a meal.

Dosage Schedule

Body Weight Ranges (kg)	Lotilaner Content per Tablet (mg)	Tablets to be Administered
0.9 to 2.0	12	One
>2.0 to 8.0	48	One
>8.0	Administer the appropriate combination of tablets	

Canada has highly variable distribution and abundance of fleas and ticks due to climate variations across the country. Consequently, a comprehensive plan, based on regional risk assessment, is recommended to determine an appropriate duration of treatment.

Flea Treatment and Prevention

Treatment with CREDELIO CAT 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.

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

Tick Treatment and Control

Treatment with CREDELIO CAT may begin at any time of year and continuing monthly through the end of tick season.

CONTRAINDICATIONS

There are no known contraindications for the use of CREDELIO CAT.

CAUTIONS

Lotilaner is a member of the isoxazoline class. This class has been associated with neurological adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in cats receiving isoxazoline class drugs, even in cats without a history of seizures. Use with caution in cats with a history of seizures or neurological disorders.

Safety and efficacy have been studied in cats aged 8 weeks and older with a body weight of 0.7 kg or more. Therefore, use of CREDELIO CAT in kittens younger than 8 weeks of age or less than 0.7 kg of body weight should be based on a benefit-risk assessment by the veterinarian.

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

WARNINGS

Wash hands after handling the product. Keep out of reach of children.

ADVERSE REACTIONS

Although all adverse reactions are not reported, the following information is based on voluntary post-approval drug experience reporting. It is generally recognized that this results in significant under-reporting. The adverse events listed here reflect reporting and not necessarily causality. Adverse events are listed by body system, in decreasing order of frequency: Skin and appendages disorders: pruritus; Behavioural disorders: hyperactivity; Systemic disorders: lethargy, anorexia; Respiratory disorders: tachypnea; Digestive tract disorders: emesis and Neurological disorders: ataxia.

For Adverse Reactions reported in a U.S. field study, see SAFETY section, Table 1.

To report suspected adverse drug events or for technical assistance, contact Elanco Canada Limited at 1-800-265-5475.

PHARMACOLOGY

Mode of Action

Lotilaner inhibits insect and acarine gamma-aminobutyric acid (GABA)-gated chloride channels. This inhibition blocks the transfer of chloride ions across cell membranes, which results in uncontrolled neuromuscular activity leading to death of insects and acarines. Lotilaner has selective activity on insects and acarines GABA receptors *versus* mammalian GABA receptors.

Pharmacokinetics

Following oral administration at 6 mg/kg (minimum recommended dose) in a pivotal pharmacokinetic study, lotilaner showed a dose-normalized (to 1 mg/kg) Cmax of 403 ng/mL, Tmax of 0.17 days (4 hours) and a half-life of 33.6 days. The bioavailability was 106% in the fed group and was 8.4% in the fasted group. Due to reduced drug bioavailability in the fasted state, CREDELIO CAT must be administered with a meal or within 30 minutes after feeding.

Following oral administration of 26 mg/kg in a margin-of-safety study, peak lotilaner concentrations were achieved in most cats at the 24-hour sampling point. Cats 3 months of age had a shorter elimination half-life (average of 7.5 days) than at 7 months of age (average of 32 days). Blood concentrations of lotilaner confirmed systemic exposure in all cats treated with the drug, although the exposure was less than proportional with increasing doses. Accumulation was observed for lotilaner as for other isoxazolines and was not associated with clinical effects.

SAFETY

In a margin of safety study, CREDELIO CAT was administered orally to 24 (8 cats/group) 8-week-old cats at 1, 3 and 5X the maximum dose of 26 mg/kg every 28 days for eight consecutive monthly doses. The 8 cats in the control group (0X) were untreated.

There were no clinically-relevant, treatment-related effects in the daily clinical observations, food consumption (wet), coagulation, clinical chemistry or urinalysis parameters, ophthalmoscopic, and physical and neurological examinations, gross examinations, microscopic observations or organ weights. Food consumption (dry food) was reduced in male cats in all treated groups compared to control correlating with a body weight decrease in the males treated at 3X only. This was considered most likely incidental to treatment since it was not seen at the higher doses in males or in females at any dose level. Upon hematology analysis, mild statistically significant decreases in neutrophils were observed in male and female at multiple time points (Day 8 through 223) at all dose levels in comparison with control, concluded not adverse as lacking consistency over time and in both genders.

In a well-controlled U.S. field study, which included 341 cats (228 cats treated with CREDELIO CAT and 113 cats treated with a topical active control), there were no serious adverse reactions related to the treatment.

Table 1: Cats with Adverse Reactions in the Field Study

Adverse Reaction (AR)	CREDELIO CAT Group: Number (and Percent) of Cats with the AR (n=228)	Active Control Group: Number (and Percent) of Cats with the AR (n=113)
Weight Loss	5 (2.2%)	2 (1.8%)
Tachypnea	3 (1.3%)	0 (0.0%)
Vomiting	3 (1.3%)	1 (0.9%)
Diarrhea	2 (0.9%)	0 (0.0%)
Anorexia	2 (0.9%)	0 (0.0%)
Elevated blood urea nitrogen (BUN)*	2 (0.9%)	0 (0.0%)

*During the study two geriatric cats developed mildly elevated blood urea nitrogen (BUN) (42 to 58 mg/dL; reference range: 14 to 36 mg/dL). One of these cats, which had suspected pre-existing kidney disease, also developed a mildly elevated serum creatinine (2.5 mg/dL; reference range: 0.6 to 2.4 mg/dL), which returned to normal by the end of the study.

EFFICACY

In a well-controlled laboratory study, CREDELIO CAT began to kill fleas six hours after administration, with greater than 98% of fleas killed within 12 hours after administration. In a well-controlled laboratory study, CREDELIO CAT demonstrated 100% effectiveness against adult fleas 24 hours after administration or infestation for 36 days.

In a 90-day well-controlled U.S. field study conducted in cats with existing flea infestations of varying severity, the efficacy of CREDELIO CAT against fleas (evaluated on Days 30, 60 and 90 compared to baseline) was 98.5%,100% and 100%, respectively. Cats with clinical signs of flea allergy dermatitis showed a significant improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermatitis, and pruritus as a direct result of eliminating fleas.

In a well-controlled laboratory study, CREDELIO CAT killed fleas before they could lay eggs, thus preventing subsequent flea infestations after the start of treatment of existing flea infestations for 30 days.

In two well-controlled laboratory studies, CREDELIO CAT demonstrated an efficacy of ≥97% against *Ixodes scapularis* ticks 72 hours after administration or infestation for 31 days.

Palatability

In the U.S. field study, owners were able to administer 99.5% of CREDELIO CAT monthly doses over three consecutive months. Out of the 648 doses administered to 225 cats 21.1% of doses were voluntarily consumed (*i.e*. when offered by hand, on the floor or in an empty bowl), 25.8% of doses were voluntarily consumed when offered with

food, and 52.6% of doses required placement of the chewable tablet in the back of the cat's mouth. Owners were unable to administer CREDELIO CAT for 0.5% of doses.

STORAGE CONDITIONS

Store between 15°C and 25°C. Excursions permitted between 5°C and 40°C.

HOW SUPPLIED

The product is available in two strengths: 12 mg and 48 mg lotilaner per tablet. Each chewable tablet strength is in colour-coded packages of 1, 3 or 6 flavoured chewable tablets. Not all package sizes may be marketed.

MANUFACTURED FOR

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<Elanco Logo>