Credelio™ CAT (lotilaner)

Chewable Tablets

For oral use in cats

Caution:
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:
CREDELIO CAT (lotilaner) is a chewable tablet for oral administration to cats and kittens according to their weight. Each chewable tablet is formulated to provide a minimum lotilaner dosage of 2.7 mg/lb (6 mg/kg).

Lotilaner has the chemical composition of 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.

Indications:
CREDELIO CAT kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) for one month in cats and kittens 8 weeks of age and older, and weighing 2.0 pounds or greater.

CREDELIO CAT is also indicated for the treatment and control of *Ixodes scapularis* (black-legged tick) infestations for one month in cats and kittens 6 months of age and older, and weighing 2.0 pounds or greater.

Dosage and Administration:
CREDELIO CAT is given orally once a month, at the minimum dosage of 2.7 mg/lb (6 mg/kg).

Dosage Schedule:

Body Weight	Lotilaner Per Chewable Tablet (mg)	Chewable Tablets Administered
2.0 to 4.0 lbs	12	One
4.1 to 17.0 lbs	48	One
Over 17.0 lbs	NA	Administer the appropriate combination of chewable tablets

NA = not applicable.

CREDELIO CAT must be administered with food (see **Clinical Pharmacology**).

Treatment with CREDELIO CAT can begin at any time of the year and can continue year-round without interruption.

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

Warnings:
Not for human use. Keep this and all drugs out of the reach of children.

Keep CREDELIO CAT in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

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

The safety of CREDELIO CAT has not been established in breeding, pregnant and lactating cats (see **Foreign Market Experience**).

The effectiveness of CREDELIO CAT against *Ixodes scapularis* in kittens less than 6 months of age has not been evaluated.

Adverse Reactions:
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.

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%)

*Two geriatric cats developed mildly elevated blood urea nitrogen (BUN) (42 to 58 mg/dL; reference range: 14 to 36 mg/dL) during the study. 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) during the study.

Foreign Market Experience: The following adverse events were reported voluntarily during post-approval use of the product in cats in foreign markets: hyperactivity, pruritus, tachypnea, dyspnea, lethargy, vomiting, anorexia, hyperthermia, hypersalivation, tachycardia, mydriasis, tremors, ataxia, seizures, hepatopathy, anaphylactic reactions resulting in death, pancreatitis, immune mediated hemolytic anemia, and glomerulopathy.

Five 3- to 4-week-old nursing kittens (one litter of 2 kittens and one litter of 3) died within three days of the queens receiving CREDELIO CAT. Two pregnant cats spontaneously aborted or had fetal and perinatal deaths within a few days of receiving CREDELIO CAT.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US, Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

Clinical Pharmacology:
Following oral administration of 26 mg/kg (the maximum labeled dose), 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). Due to reduced drug bioavailability in the fasted state, CREDELIO CAT must be administered with a meal or within 30 minutes after feeding.

Mode of Action:
Lotilaner is an ectoparasiticide belonging to the isoxazoline group. 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. The selective toxicity of lotilaner between insects and acarines and mammals may be inferred by the differential sensitivity of the insects and acarines' GABA receptors versus mammalian GABA receptors.

Effectiveness:
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 another well-controlled laboratory study, CREDELIO CAT demonstrated 100% effectiveness against adult fleas 24 hours after administration or infestation for 35 days.

In a 90-day well-controlled U.S. field study conducted in cats with existing flea infestations of varying severity, the effectiveness of CREDELIO CAT against fleas on Days 30, 60 and 90 compared to baseline was 98.5%,100% and 100%, respectively. Cats with signs of flea allergy dermatitis showed 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 well-controlled laboratory studies, CREDELIO CAT demonstrated >97% effectiveness against *Ixodes scapularis* ticks 72 hours after administration or infestation for 31 days.

Palatability: In the U.S. field study, which included 648 doses administered to 225 cats, 21.1% of the doses were voluntarily consumed when CREDELIO CAT was offered by hand, on the floor, or in an empty bowl, an additional 25.8% of doses were voluntarily consumed when CREDELIO CAT was 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.

Animal 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 labeled dose of 26 mg/kg every 28 days for eight consecutive doses. The 8 cats in the control group (0X) were untreated.

There were no clinically-relevant, treatment-related effects on physical and neurologic examinations or gross pathology. Dry food consumption was reduced in male cats in all treated groups compared to control cats. Body weights of male cats in the 3X group were less than the control male cats. Vomiting occurred post-dosing in cats in all groups, including the control group, but was increased in the 5X group. At multiple time points, neutrophil counts were decreased (750-2710/µL; low end of normal: approximately 2800/µL) in cats in all treated groups compared to control cats, including in a cat in the 3X group that died during anesthesia to obtain the electrocardiogram (ECG). From Days 28 to 92, two and three female cats in the 3X and 5X group, respectively, had elevations in blood urea nitrogen (BUN) at least at one time point (37-43 mg/dL; high end of normal: 36 mg/dL). Three cats each in the control, 1X and 5X groups and six cats in the 3X group had minimal, usually unilateral, tubular regeneration of the kidneys. One cat each in the control, 1X and 5X groups and four cats in the 3X group had minimal generalized lymphoid depletion of the thymus. Four of the five cats in the two high-dose groups (3X and 5X) with the thymus changes also had neutropenia at 25% or more of the time points.

Blood concentrations of lotilaner confirmed systemic exposure in all cats administered lotilaner, although the exposure was less than dose proportional.

Storage Information:
Store at 15-25°C (59 -77°F), excursions permitted between 5 to 40°C (41 to 104°F).

How Supplied:

CREDELIO CAT is available in two chewable tablet sizes for use in cats: 12 and 48 mg lotilaner. Each chewable tablet size is available in color-coded packages containing 1 chewable tablet. The 48 mg chewable tablet size is also available in color-coded packages containing 3 or 6 chewable tablets.

Approved by FDA under NADA # 141-528

Manufactured for:
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Greenfield, IN 46140 USA

CredelioCAT.com

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