

# HI, I'M CREDELIO

## GENTLE ON DOGS, TOUGH ON TICKS & FLEAS

GENTLE IS MY MIDDLE NAME



  
**Credelio**<sup>®</sup>  
(lotilaner)

**GENTLE & TOUGH**

# I PROTECT DOGS OF ALL SIZES

## BIG, SMALL, MEDIUM AND SMEDIUM



From Chihuahuas to Mastiffs and every breed in between, Credelio® (lotilaner) is designed to be gentle on all dogs 4.4 pounds or more, as young as 8 weeks old. But, you know what it's not gentle on? Ticks and fleas—it starts killing them\* ruthlessly in just 4 hours.<sup>1,2</sup> That's powerful protection for your pup. See product label on page 8 for complete safety information.

*\*I. ricinus, C. felis*

# TICKS

## TARGET EVERY MEMBER OF YOUR FAMILY—FURRY OR OTHERWISE.

Here are five reasons why you should always take ticks seriously:

### 1. Ticks can be lethal.

They can spread many diseases, like babesiosis, Rocky Mountain spotted fever and Lyme disease, some of which are **debilitating or even deadly to you and your dog.**<sup>1</sup>

### 2. Ticks work hard.

No, really. They find hosts through a process called questing.<sup>1,2</sup> They climb up tall vegetation, **wave their front legs back and forth and when animals like your dog walk by, they grab hold, latch on and feed.**

### 3. Ticks are strong.

They secrete a glue-like substance to firmly secure their mouthparts in your dog's skin.<sup>5,6</sup> To remove a tick, wear gloves and use tweezers to grasp it close to your dog's skin. Extract it using steady rearward pressure.<sup>1</sup> **Don't twist, jerk or crush a tick.** If you do, you may leave its mouthparts in your dog's skin, which increases the risk of infection and disease.<sup>3</sup>

### 4. Ticks look for the perfect place to eat.

Ticks latch onto your dog to feed on his blood. **Sometimes they detach, search for a new location on your dog and reattach to feed again,** eventually settling on a single location for a large blood meal.<sup>4</sup>

### 5. Ticks can make your home, their home.

*Rhipicephalus sanguineus*, more commonly known as the brown dog tick, is the most widespread tick in the world.<sup>7</sup> It's also the **only species adapted to live and reproduce indoors.**<sup>4</sup>

# FLEAS

## ARE MORE THAN JUST ANNOYING.

Fleas are cunning little critters. Here are a few things to remember when dealing with them:

### 1. Fleas can be anywhere.

**They could be at the dog kennel, in your garage, between the cracks of your hardwood floors and all over your backyard.** They can also live on opossums, raccoons, skunks and other wild animals. When these kinds of animals pass through your yard, they can drop flea eggs, which develop into adults that can hop onto your unsuspecting dog.<sup>6</sup>

### 2. Fleas hold their ground.

**Once an adult flea lands on your dog, it plans to stay there.** Fleas don't search for new hosts once they have one.<sup>8</sup> If a flea jumps on your dog, chances are it's staying there.

### 3. Fleas act fast.

Females begin laying eggs 20–24 hours after their first blood meal and can lay about 2,000 in their lifetime.<sup>9</sup> You may not see fleas right away, but numbers can increase rapidly as thousands of eggs develop in the environment. This high volume makes it **critical to kill fleas before they lay eggs.**

### 4. Fleas can be difficult to spot.

In mild infestations, **you may not see fleas on your dog.** You might, however, find small black pellets of "flea dirt" (flea feces with partially digested blood) in your dog's fur. In moderate and severe infestations, you might see adult fleas crawling on your dog's skin.<sup>8</sup>

### 5. Fleas use dogs to spread infections.

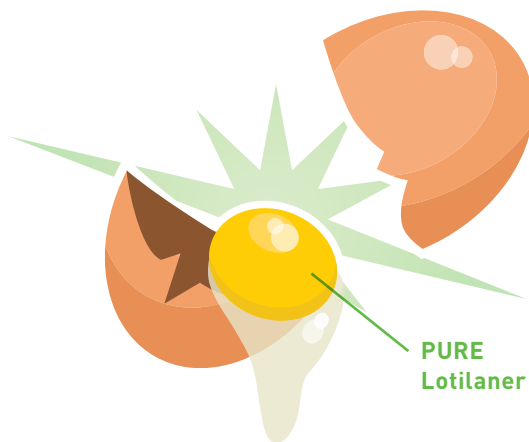
Fleas pose serious risks to your dog including tapeworm infection, bartonellosis (cat-scratch fever) and other diseases and conditions **that can affect your dog, other pets and your family.**<sup>8</sup>

# EXTRA PURIFIED

Have you ever read a recipe and wondered if all of the ingredients are really necessary? Does every ingredient play a pivotal role in the dish?

In the recipe for some medications, the active ingredient is a mixture of different forms of the molecule. When creating Credelio® (lotilaner), Elanco discovered that only one part of the mixture was necessary to get the desired effect. So Elanco takes the extra step to filter out the part of the mixture that isn't needed, leaving only lotilaner, the purified active ingredient, which means your dog only takes what he needs.

Imagine you were making a recipe that only called for an egg yolk. So, would you include the whole egg when only the yolk is needed? Think of lotilaner as the egg yolk in the egg. Credelio uses only the part you need and not what you don't.



Credelio only includes what it needs, and removes the rest.

Some may argue that this extra purification step isn't necessary, that as long as the active ingredient is there in the mixture, you'll get the same outcome. Elanco thinks differently.

## CREDELIO'S EXTRA PURIFICATION PROCESS OFFERS THREE BENEFITS:



Decreased possibility of potential side effects.<sup>12</sup>



There's less for your dog's body to process.<sup>11</sup>



Your dog gets strong protection in a smaller tablet that's easy to give.<sup>11</sup>

## GENTLE BY DESIGN

Credelio's extra purification process keeps only what it needs—lotilaner—and removes the rest. The final product is a small, tasty<sup>10</sup> chewable that's gentle by design, and provides tough tick and flea protection that's gentle on dogs. See product label on page 8 for complete safety information.





# ASK YOUR VETERINARIAN TODAY

## Indications

Credelio kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) and the treatment and control of tick infestations [*Amblyomma americanum* (lone star tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick) and *Rhipicephalus sanguineus* (brown dog tick)] for one month in dogs and puppies 8 weeks of age and older, and weighing 4.4 pounds or greater.

## Important Safety Information

Lotilaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, incoordination, and seizures. Seizures have been reported in dogs receiving this class of drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders. The safe use of Credelio in breeding, pregnant or lactating dogs has not been evaluated. The most frequently reported adverse reactions are weight loss, elevated blood urea nitrogen, increased urination, and diarrhea. For complete safety information, please see Credelio product label or ask your veterinarian.

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2. Murphy, M. et al. 2017. "Laboratory evaluation of the speed of kill of lotilaner (Credelio™) against Ixodes ricinus ticks on dogs." *Parasites & Vectors*. 10:541.
3. Companion Animal Parasite Council. "Ticks for dog." <https://www.capcvet.org/guidelines/ticks/>. Updated April 12, 2017.
4. Dryden, MW. and Payne, P. 2004. "Biology and control of ticks infesting dogs and cats in North America." *Vet. Ther.* 5.2:139-154.
5. Suppan, J. et al. 2017. "Tick attachment cement: reviewing the mysteries of a biological skin plug system." *Biol. Rev. Camb. Philos. Soc.* <http://onlinelibrary.wiley.com/doi/10.1111/brv.12384/epdf>. Accessed November 10, 2017.
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7. Dantas-Torres F. 2010. "Biology and ecology of the brown dog tick, *Rhipicephalus sanguineus*." *Parasites & Vectors*. 3:26-36.
8. Dryden, M. et al. 2005 guidelines: flea control for dogs and cats. Advanstar Veterinary Healthcare Communications.
9. Companion Animal Parasite Council. "Fleas for dog." <https://www.capcvet.org/guidelines/fleas/>. Updated September 19, 2017.
10. Karadzovska, D. et al. 2017. "A randomized, controlled field study to assess the efficacy and safety of lotilaner flavored chewable tablets (Credelio™) in eliminating fleas in client-owned dogs in the USA." *Parasites & Vectors*. 10:528.
11. Toutain, C, Seewald W, Jung M. The intravenous and oral pharmacokinetics of lotilaner in dogs. *Parasites and Vectors*. 2017;10:522.
12. Development of New Stereoisomeric Drugs.pdf <https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm122883.htm>. Updated March 21, 2018.

**Credelio**  
(lotilaner)

## Chewable Tablets

For oral use in dogs

### Caution:

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

### Description:

CREDELIO (lotilaner) is a beef-flavored, chewable tablet for oral administration to dogs and puppies according to their weight. Each chewable tablet is formulated to provide a minimum lotilaner dosage of 9 mg/lb (20 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 kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) and the treatment and control of tick infestations [*Amblyomma americanum* (lone star tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick) and *Rhipicephalus sanguineus* (brown dog tick)] for one month in dogs and puppies 8 weeks of age and older, and weighing 4.4 pounds or greater.

### Dosage and Administration:

CREDELIO is given orally once a month, at the minimum dosage of 9 mg/lb (20 mg/kg).

### Dosage Schedule:

Body Weight	Lotilaner Per Chewable Tablet (mg)	Chewable Tablets Administered
4.4 to 6.0 lbs	56.25	One
6.1 to 12.0 lbs	112.5	One
12.1 to 25.0 lbs	225	One
25.1 to 50.0 lbs	450	One
50.1 to 100.0 lbs	900	One
Over 100.0 lbs	Administer the appropriate combination of chewable tablets	

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

Treatment with CREDELIO 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.

### Warnings:

Not for human use. Keep this and all drugs out of the reach of children. Keep CREDELIO 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. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders. The safe use of CREDELIO in breeding, pregnant or lactating dogs has not been evaluated.

**Adverse Reactions:**

In a well-controlled U.S. field study, which included 284 dogs (198 dogs treated with CREDELIO and 86 dogs treated with an oral active control), there were no serious adverse reactions.

Over the 90-day study period, all observations of potential adverse reactions were recorded. Reactions that occurred at an incidence of 1% or greater are presented in the following table.

**Dogs with Adverse Reactions in the Field Study:**

Adverse Reaction (AR)	CREDELIO Group: Number (and Percent) of Dogs with the AR (n=198)	Active Control Group: Number (and Percent) of Dogs with the AR (n=86)
Weight Loss	3 (1.5%)	2 (2.3%)
Elevated Blood Urea Nitrogen (BUN)	2 (1.0%)*	0 (0.0%)
Polyuria	2 (1.0%)*	0 (0.0%)
Diarrhea	2 (1.0%)	2 (2.3%)

\*Two geriatric dogs developed mildly elevated BUN (34 to 54 mg/dL; reference range: 6 to 31 mg/dL) during the study. One of these dogs also developed polyuria and a mildly elevated potassium (6.5 mEq/L; reference range: 3.6 to 5.5 mEq/L) and phosphorous (6.4 mg/dL; reference range: 2.5 to 6.0 mg/dL). The other dog also developed a mildly elevated creatinine (1.7 to 2.0 mg/dL; reference range: 0.5 to 1.6 mg/dL) and weight loss.

In addition, one dog experienced intermittent head tremors within 1.5 hours of administration of vaccines, an ear cleaning performed by the owner, and its first dose of CREDELIO. The head tremors resolved within 24 hours without treatment. The owner elected to withdraw the dog from the study.

In an Australian field study, one dog with a history of seizures experienced seizure activity (tremors and glazed eyes) six days after receiving CREDELIO. The dog recovered without treatment and completed the study. In the U.S. field study, two dogs with a history of seizures received CREDELIO and experienced no seizures throughout the study.

In three well-controlled European field studies and one U.S. laboratory study, seven dogs experienced episodes of vomiting and four dogs experienced episodes of diarrhea between 6 hours and 3 days after receiving CREDELIO.

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/AnimalVeterinary/SafetyHealth>.

**Clinical Pharmacology:**

Following oral administration of 43 mg/kg (approximately 1X the maximum labeled dose), peak lotilaner concentrations were achieved between 6 hours and 3 days in dogs 2 months of age and between 1 and 7 days in dogs 10 months of age. Dogs 2 months of age had a shorter elimination half-life (average of 9.6 days) than at 10 months of age (average of 28.4 days). Due to reduced drug bioavailability in the fasted state, CREDELIO 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 well-controlled European laboratory studies, CREDELIO began to kill fleas four hours after administration or infestation, with greater than 99% of fleas killed within eight hours after administration or infestation for 35 days. In a well-controlled U.S. laboratory study, CREDELIO demonstrated 100% effectiveness against adult fleas 12 hours after administration or infestation for 35 days.

In a 90-day well-controlled U.S. field study conducted in households with existing flea infestations of varying severity, the effectiveness of CREDELIO against fleas on Days 30, 60 and 90 compared to baseline was 99.5%, 100% and 100%, respectively. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus as a direct result of eliminating fleas.

In well-controlled laboratory studies, CREDELIO demonstrated > 97% effectiveness against *Amblyomma americanum*, *Dermacentor variabilis*, *Ixodes scapularis* and *Rhipicephalus sanguineus* ticks 48 hours after administration or infestation for 30 days. In a well-controlled European laboratory study, CREDELIO started killing *Ixodes ricinus* ticks within four hours after administration.

**Palatability:**

In the U.S. field study, which included 567 doses administered to 198 dogs, 80.4% of dogs voluntarily consumed CREDELIO when offered by hand or in an empty bowl, an additional 13.6% consumed CREDELIO when offered with food, and 6.0% required placement of the chewable tablet in the back of the dog's mouth.

**Animal Safety:**

In a margin of safety study, CREDELIO was administered orally to 24 (8 dogs/group) 8-week-old Beagle puppies at doses of 43 mg/kg, 129 mg/kg, and 215 mg/kg (approximately 1, 3, and 5X the maximum labeled dose, respectively) every 28 days for eight consecutive doses. The 8 dogs in the control group (0X) were untreated. There were no clinically-relevant, treatment-related effects on clinical observations, physical and neurological examinations, body weights, food consumption, electrocardiograms, clinical pathology (hematology, clinical chemistries, coagulation profiles and urinalysis), gross pathology, histopathology, or organ weights. Blood concentrations of lotilaner confirmed systemic exposure of all treated dogs, although the exposure was less than dose proportional at 5X.

In a well-controlled field study, CREDELIO was used concurrently with other medications, such as vaccines, anthelmintics, antibiotics, steroids, NSAIDs, anesthetics, and antihistamines. No adverse reactions were observed from the concomitant use of CREDELIO with other medications.

**Storage Information:**

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

**How Supplied:**

CREDELIO is available in five chewable tablet sizes for use in dogs: 56.25, 112.5, 225, 450, and 900 mg lotilaner.

Each chewable tablet size is available in color-coded packages of 1 or 6 chewable tablets.

Approved by FDA under NADA # 141-494

Manufactured for:

Elanco US Inc  
Greenfield, IN 46140 USA  
Credelio.com

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Rev. date 09/2019  
PA280144X W1b

# BIG SAVINGS

# FROM YOUR DOG'S FAVORITE DEFENDER



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Talk to your veterinarian about the gentle yet tough protection of Credelio® (lotilaner).



**Sign up for text or email dosing reminders at  
Credelio.com**



**24/7 support available at 888-545-5973**

\*Savings in the form of a rebate. Rebate provided on a Credelio® (lotilaner) Visa® Prepaid Card. Card is issued by MetaBank®, Member FDIC, pursuant to a license from Visa U.S.A. Inc. No cash access or recurring payments. Can be used everywhere Visa debit cards are accepted. Card valid for up to 6 months; unused funds will forfeit after the valid thru date. Card terms and conditions apply. Offer valid for purchases dated 1/1/20-6/30/20. Rebate request must be postmarked or submitted on or before 9/30/2020. For mail-in submissions, send a copy of your veterinary invoice with your name and address and rebate form to Elanco Rebates, PO Box 540031, El Paso, TX 88554. For rebate questions call 844-408-8476.

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PM-US-19-0321(2)



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