CREDELIO- lotilaner tablet, chewable
Elanco US Inc.

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/reportanimalae.

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/pyodermatitis and pruritus as a direct result of eliminating fleas.

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

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, 3 or 6 chewable tablets.

Approved by FDA under NADA # 141-494

Manufactured for:
Elanco US Inc
Greenfield, IN 46140 USA
Credelio.com

Rev. date 05/2020
PA102967X

Elanco™

Principal Display Panel - 3 Tablets 56.25 mg Box Label

3 Tablets

Dogs &
puppies

4.4-6.0 lbs

Credelio™
(lotilaner)

For the treatment and
prevention of flea infestations
and for the treatment and control
of tick infestations in dogs and
puppies 8 weeks of age and older

56.25 mg chewable tablet

Kills fleas

Kills ticks

Monthly dose

Give with
food

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

Approved by FDA under NADA # 141-494

Elanco™

Principal Display Panel - 3 Tablets 112.5 mg Box Label

3 Tablets

Dogs &
puppies

6.1-12.0 lbs

Credelio™
(lotilaner)

For the treatment and
prevention of flea infestations
and for the treatment and control
of tick infestations in dogs and
puppies 8 weeks of age and older

112.5 mg chewable tablet

Kills fleas

Kills ticks

Monthly dose

Give with
food

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

Approved by FDA under NADA # 141-494

Elanco™

Principal Display Panel - 3 Tablets 225 mg Box Label

3 Tablets

Dogs &
puppies

12.1-25.0 lbs

Credelio™
(lotilaner)

For the treatment and
prevention of flea infestations
and for the treatment and control
of tick infestations in dogs and
puppies 8 weeks of age and older

225 mg chewable tablet

Kills fleas

Kills ticks

Monthly dose

Give with
food

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

Approved by FDA under NADA # 141-494

Elanco™

Principal Display Panel - 3 Tablets 450 mg Box Label

3 Tablets

Dogs &
puppies

25.1-50.0 lbs

Credelio™
(lotilaner)

For the treatment and
prevention of flea infestations
and for the treatment and control
of tick infestations in dogs and
puppies 8 weeks of age and older

450 mg chewable tablet

Kills fleas

Kills ticks

Monthly dose

Give with
food

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

Approved by FDA under NADA # 141-494

Elanco™

Principal Display Panel - 3 Tablets 900 mg Box Label

3 Tablets

Dogs &
puppies

50.1-100.0 lbs

Credelio™
(lotilaner)

For the treatment and
prevention of flea infestations
and for the treatment and control
of tick infestations in dogs and
puppies 8 weeks of age and older

900 mg chewable tablet

Kills fleas

Kills ticks

Monthly dose

Give with
food

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

Approved by FDA under NADA # 141-494

Elanco™

CREDELIO

lotilaner tablet, chewable

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:58198-5452
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Lotilaner (UNII: HEH4938D7K) (Lotilaner - UNII:HEH4938D7K)	Lotilaner	56.25 mg

Product Characteristics			
Color	White (beige with brownish spots)	**Score**	no score
Shape	ROUND (biconvex beveled edges)	**Size**	7mm
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:58198-5452-3	16 in 1 BOX		
1	NDC:58198-5452-1	1 in 1 CARTON		
1		1 in 1 BLISTER PACK		
2	NDC:58198-5452-4	10 in 1 BOX		
2	NDC:58198-5452-2	2 in 1 CARTON		
2		3 in 1 BLISTER PACK		
3	NDC:58198-5452-5	7 in 1 BOX		
3		1 in 1 CARTON		
3		1 in 1 BLISTER PACK		
4	NDC:58198-5452-6	16 in 1 BOX		
4	NDC:58198-5452-7	1 in 1 CARTON		
4		3 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141494	01/19/2018	

CREDELIO

lotilaner tablet, chewable

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:58198-5458
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**

Lotilaner (UNII: HEH4938D7K) (Lotilaner - UNII:HEH4938D7K)	Lotilaner	112.5 mg

Product Characteristics

Color	White (beige with brownish spots)	**Score**	no score
Shape	ROUND (biconvex beveled edges)	**Size**	9mm
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-5458-3	16 in 1 BOX		
1	NDC:58198-5458-1	1 in 1 CARTON		
1		1 in 1 BLISTER PACK		
2	NDC:58198-5458-4	10 in 1 BOX		
2	NDC:58198-5458-2	2 in 1 CARTON		
2		3 in 1 BLISTER PACK		
3	NDC:58198-5458-5	7 in 1 BOX		
3		1 in 1 CARTON		
3		1 in 1 BLISTER PACK		
4	NDC:58198-5458-6	16 in 1 BOX		
4	NDC:58198-5458-7	1 in 1 CARTON		
4		3 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141494	01/19/2018	

CREDELIO

lotilaner tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:58198-5456
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Lotilaner (UNII: HEH4938D7K) (Lotilaner - UNII:HEH4938D7K)	Lotilaner	225 mg

Product Characteristics

Color	White (beige with brownish spots)	**Score**	no score

Shape	ROUND (biconvex beveled edges)	**Size**	12mm
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-5456-3	16 in 1 BOX		
1	NDC:58198-5456-1	1 in 1 CARTON		
1		1 in 1 BLISTER PACK		
2	NDC:58198-5456-4	10 in 1 BOX		
2	NDC:58198-5456-2	2 in 1 CARTON		
2		3 in 1 BLISTER PACK		
3	NDC:58198-5456-5	7 in 1 BOX		
3		1 in 1 CARTON		
3		1 in 1 BLISTER PACK		
4	NDC:58198-5456-6	16 in 1 BOX		
4	NDC:58198-5456-7	1 in 1 CARTON		
4		3 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141494	01/19/2018	

CREDELIO

lotilaner tablet, chewable

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:58198-5454
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Lotilaner (UNII: HEH4938D7K) (Lotilaner - UNII:HEH4938D7K)	Lotilaner	450 mg

Product Characteristics

Color	White (beige with brownish spots)	**Score**	no score
Shape	ROUND (biconvex beveled edges)	**Size**	15mm
Flavor		**Imprint Code**	
Contains			

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-5454-3	16 in 1 BOX		
1	NDC:58198-5454-1	1 in 1 CARTON		
1		1 in 1 BLISTER PACK		
2	NDC:58198-5454-4	10 in 1 BOX		
2	NDC:58198-5454-2	2 in 1 CARTON		
2		3 in 1 BLISTER PACK		
3	NDC:58198-5454-6	16 in 1 BOX		
3	NDC:58198-5454-7	1 in 1 CARTON		
3		3 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141494	01/19/2018	

CREDELIO

lotilaner tablet, chewable

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:58198-5451
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
Lotilaner (UNII: HEH4938D7K) (Lotilaner - UNII:HEH4938D7K)	Lotilaner	900 mg

Product Characteristics			
Color	White (beige with brownish spots)	**Score**	no score
Shape	ROUND (biconvex beveled edges)	**Size**	19mm
Flavor		**Imprint Code**	
Contains			

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:58198-5451-3	16 in 1 BOX		
1	NDC:58198-5451-1	1 in 1 CARTON		
1		1 in 1 BLISTER PACK		
2	NDC:58198-5451-4	10 in 1 BOX		
2	NDC:58198-5451-2	2 in 1 CARTON		
2		3 in 1 BLISTER PACK		

3	NDC:58198-5451-6	16 in 1 BOX		
3	NDC:58198-5451-7	1 in 1 CARTON		
3		3 in 1 BLISTER PACK		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141494	01/19/2018	

Labeler - Elanco US Inc. (966985624)

Establishment

Name	Address	ID/FEI	Business Operations
Siegfried AG		482824026	API MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Siegfried (Nantong) Pharmaceuticals Co., Ltd.		421329766	API MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Elanco France SAS		736833104	MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Allpack		484572565	LABEL, PACK

Establishment

Name	Address	ID/FEI	Business Operations
Elanco Clinton Laboratories		039138631	PACK, LABEL

Revised: 8/2021 Elanco US Inc.