ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio Plus 112.5 mg/4.22 mg chewable tablets for dogs (> 2.8–5.5 kg)

lotilaner/milbemycin oxime

2. STATEMENT OF ACTIVE SUBSTANCES

112.5 mg lotilaner/4.22 mg milbemycin oxime

3. PHARMACEUTICAL FORM

Chewable tablet

4. PACKAGE SIZE

1 tablet
3 tablets
6 tablets
18 tablets

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Administer with or after food.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann Strasse 4
Groden
D-27472 Cuxhaven
Germany

16. MARKETING AUTHORISATION NUMBER(S)

Vm 52127/5034

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio Plus 112.5 mg/4.22 mg (> 2.8–5.5 kg)

lotilaner/milbemycin oxime (EN or Latin)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco

3. EXPIRY DATE

EXP {month/year}

4. BATCH NUMBER

Lot {number}

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

Credelio Plus 56.25 mg/2.11 mg chewable tablets for dogs (1.4–2.8 kg)
Credelio Plus 112.5 mg/4.22 mg chewable tablets for dogs (> 2.8–5.5 kg)
Credelio Plus 225 mg/8.44 mg chewable tablets for dogs (> 5.5–11 kg)
Credelio Plus 450 mg/16.88 mg chewable tablets for dogs (> 11–22 kg)
Credelio Plus 900 mg/33.75 mg chewable tablets for dogs (> 22–45 kg)

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

Elanco GmbH
Heinz-Lohmann Strasse 4
Groden
D-27472 Cuxhaven
Germany

Manufacturer responsible for batch release:

Elanco France S.A.S
26 Rue de la Chapelle
68330 Huningue
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Credelio Plus 56.25 mg/2.11 mg chewable tablets for dogs (1.4–2.8 kg)
Credelio Plus 112.5 mg/4.22 mg chewable tablets for dogs (> 2.8–5.5 kg)
Credelio Plus 225 mg/8.44 mg chewable tablets for dogs (> 5.5–11 kg)
Credelio Plus 450 mg/16.88 mg chewable tablets for dogs (> 11–22 kg)
Credelio Plus 900 mg/33.75 mg chewable tablets for dogs (> 22–45 kg)

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each chewable tablet contains:

Credelio Plus chewable tablets	**lotilaner (mg)**	**milbemycin oxime (mg)**
for dogs (1.4–2.8 kg)	56.25	2.11
for dogs (> 2.8–5.5 kg)	112.5	4.22
for dogs (> 5.5–11 kg)	225	8.44
for dogs (> 11–22 kg)	450	16.88
for dogs (> 22–45 kg)	900	33.75

White to beige round biconvex chewable tablets with brownish spots.

4. INDICATION(S)

For use in dogs with, or at risk from, mixed infestations/infections of ticks, fleas, mites, gastrointestinal nematodes, heartworm and/or lungworm. This veterinary medicinal product is indicated for use when treatment against ticks/fleas/mites and gastrointestinal nematodes or the treatment against ticks/fleas/mites and prevention of heartworm disease/angiostrongylosis is required concurrently.

Ectoparasites
For the treatment of tick (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus* and *I. hexagonus*) and flea (*Ctenocephalides felis* and *C. canis*) infestations in dogs.

This veterinary medicinal product provides immediate and persistent killing activity for 1 month for ticks and fleas.

The veterinary medicinal product can be used as part of a treatment strategy for the control of flea allergy dermatitis (FAD).

For the treatment of demodicosis (caused by *Demodex canis*).

Gastrointestinal Nematodes
Treatment of gastrointestinal nematodes: hookworm (L4, immature adult (L5) and adult *Ancylostoma caninum*), roundworms (L4, immature adult (L5) and adult *Toxocara canis* and adult *Toxascaris leonina*) and whipworm (adult *Trichuris vulpis*).

Heartworm
Prevention of heartworm disease (*Dirofilaria immitis*).

Lungworm
Prevention of angiostrongylosis by reduction of the level of infection with immature adult (L5) and adult stages of *Angiostrongylus vasorum* (lungworm) with monthly administration.

5. CONTRAINDICATIONS

Do not use in cases of known hypersensitivity to the active substances, or to any of the excipients.

6. ADVERSE REACTIONS

Gastrointestinal signs (diarrhoea and vomiting), anorexia, muscle tremors, lethargy, pruritus and changes in behaviour were uncommonly reported. These occurrences were generally self-limiting and of short duration.Neurological signs (convulsion,

muscle tremor, and ataxia) have been recorded rarely in post-marketing safety experience for the active substance lotilaner used as a mono-active (Credelio) at the same dose as in this product. These signs typically resolve without treatment.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Oral use.
The veterinary medicinal product should be administered in accordance with the following table to ensure a dose of 20 to 41 mg lotilaner/kg bodyweight and 0.75 to 1.53 mg milbemycin oxime/kg bodyweight.

Dog bodyweight	**Strength and number of Credelio Plus tablets to be administered**				
	56.25 mg/ 2.11 mg	**112.5 mg/ 4.22 mg**	**225 mg/ 8.44 mg**	**450 mg/ 16.88 mg**	**900 mg/ 33.75 mg**
1.4–2.8 kg	1				
> 2.8–5.5 kg		1			
> 5.5–11 kg			1		
> 11–22 kg				1	
> 22–45 kg					1
> 45 kg	Appropriate combination of tablets				

9. ADVICE ON CORRECT ADMINISTRATION

Credelio Plus is a palatable chewable flavoured tablet. Administer the chewable tablet(s) with or after food.Use an appropriate combination of available strengths to achieve the recommended dose of 20–41 mg lotilaner/kg and 0.75–1.53 mg milbemycin oxime/kg for animals > 45 kg bodyweight.

The treatment schedule should be based on the individual risk assessment of the dog, the local epidemiological situation and/or the epidemiological situation of other

areas the dog has visited or is going to visit. If based on the veterinarian'**s** opinion the dog requires re-administration(s) of the product, any subsequent administration(s) must follow the 1 month interval schedule.

The product should be used in dogs with, or at risk from, mixed infestations of ectoparasites (ticks, fleas or mites) and endoparasites (gastrointestinal nematodes and/or for prevention of heartworm/lungworm). Otherwise, a narrower spectrum parasiticide should be used.

Dogs living in non-heartworm endemic areas:
The veterinary medicinal product can be used as part of the seasonal treatment of ticks and/or fleas in dogs with diagnosed, or at risk from, concurrent gastrointestinal nematode infections or at risk of lungworm. A single treatment is effective for the treatment of gastrointestinal nematodes.

Dogs living in heartworm endemic areas:
Prior to treatment with the veterinary medicinal product the advice in special warnings should be considered.

For the prevention of heartworm disease and the concurrent treatment of tick and/or flea infestations, the veterinary medicinal product must be given at regular monthly intervals during the time of the year when mosquitoes, ticks and/or fleas are present. The first dose of the veterinary medicinal product may be given after first possible exposure to mosquitoes, but not more than one month after this exposure.

When the veterinary medicinal product is used to replace another heartworm preventive product, the first dose of the product must be given within a month of the last dose of the former medication.
Dogs travelling to a heartworm region should start medication within a month after arrival there.
Heartworm prevention treatment should be continued monthly, with the last administration being given 1 month after the dog has left the region.

Lungworm:
In endemic areas, monthly administration of the veterinary medicinal product will reduce the level of infection with immature adults (L5) and adults of *Angiostrongylus vasorum* in the heart and lungs. It is recommended that lungworm prevention should be continued until at least 1 month after the last exposure to slugs and snails.

Seek veterinary advice regarding information on the optimal time to start treatment with this veterinary medicinal product.

For the treatment of demodicosis (caused by *Demodex canis*):
Monthly administration of the product for two consecutive months is efficacious and leads to a marked improvement of clinical signs. Treatment should be continued until two negative skin scrapings are obtained one month apart. Severe cases may require prolonged monthly treatments. As demodicosis is a multi-factorial disease, where possible, it is advisable to also treat any underlying disease appropriately.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store in the original package

This veterinary medicinal product does not require any special storage conditions.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and blister after EXP.

The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

Special warnings for each target species:

All dogs within the household should be treated with a suitable product.

Ticks and fleas must attach to the host and commence feeding in order to be exposed to the active substance; therefore the risk of the transmission of tick/flea-borne diseases cannot be excluded.

Parasite resistance to any particular class of anthelmintic may develop following the frequent, repeated use of an anthelmintic of that class. Therefore, the use of this veterinary medicinal product should be based on the assessment of each individual case and on local epidemiological information about the current susceptibility of the target species in order to limit the possibility of a future selection for resistance.

For the treatment of infections with gastrointestinal nematodes the need for, and the frequency of, re-treatment as well as the choice of the treatment (monosubstance or combination product) should be evaluated by the prescribing veterinarian.

Maintenance of the efficacy of macrocyclic lactones is critical for *Dirofilaria immitis* prevention, therefore, to minimise the risk of resistance selection, it is recommended that dogs should be checked for both circulating antigens and blood microfilariae at the beginning of each heartworm season prior to starting monthly preventive treatments. The product is not effective against adult *D. immitis* and is not indicated for microfilariae clearance.

Special precautions for use in animals:

All safety and efficacy data have been acquired from dogs and puppies 8 weeks of age and older and 1.4 kg of bodyweight and greater. Use of this veterinary

medicinal product in puppies younger than 8 weeks of age or less than 1.4 kg of bodyweight should be based on a benefit-risk assessment by the responsible veterinarian.

The recommended dose should be strictly observed in MDR1 mutant ($^{-/-}$) dogs with a non-functional P-glycoprotein, which may include Collies and related breeds.

Prior to first administration, dogs in heartworm endemic areas or who have visited heartworm endemic areas must be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to kill adult heartworms.

Administration of products containing milbemycin oxime (such as this product) to dogs with a high number of circulating microfilariae is not recommended in order to avoid hypersensitivity reactions associated with the release of proteins from dead or dying microfilariae.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Accidental ingestion may cause gastrointestinal disturbances. In order to prevent access by children, keep the tablets in the blister packs until required and keep the blister packs in the outer carton out of the reach of children.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or label to the physician.

Wash hands after handling the tablets.

Pregnancy and lactation:

The safety of the veterinary medicinal product in breeding, pregnant and lactating dogs has not been investigated. Laboratory studies with the active substances in rats have not produced any evidence of teratogenic effects, or any adverse effect on the reproductive capacity of males and females.

Use according to the benefit-risk assessment of the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

Lotilaner and milbemycin oxime have been shown to be a substrate for P-glycoprotein (P-gp) and therefore could interact with other P-gp substrates (e.g. digoxin, doxorubicin) or other macrocyclic lactones. Therefore, concomitant treatment with other P-gp substrates could lead to enhanced toxicity.

Overdose (symptoms, emergency procedures, antidotes):

No adverse reactions, other than those listed in this leaflet, were observed in puppies (starting at 8 - 9 weeks of age) after administering up to 5 times the maximum recommended dose over 1 - 5 days (consecutive daily dosing) at monthly intervals on 9 occasions; or in adult dogs (starting at 11 months of age)

after administering up to 5 times the maximum recommended dose over 1 - 5 days (consecutive daily dosing) at monthly intervals on 7 occasions; or in adult dogs (approximately 12 months old) after administration up to 6 times the maximum recommended dose as a bolus on a single occasion.

After administration of 5 times the maximum recommended dose to MDR1 mutant ($^{-/-}$) dogs with a non-functional P-glycoprotein, transient depression, ataxia, tremors, mydriasis and/or excessive salivation were observed.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

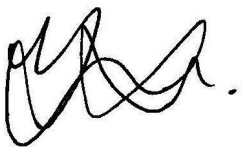
14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

February 2023

15. OTHER INFORMATION

Aluminium/aluminium blisters packaged into an outer cardboard box.
Pack sizes of 1, 3, 6 or 18 tablets.

Not all pack sizes may be marketed.



Approved: 23 February 2023